FOURTH EDITION

SKIN DISEASE

Diagnosis and Treatment

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Diagnosis and Treatment

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Topical Therapy 1

James G. H. Dinulos

Basic Principles of Treatment

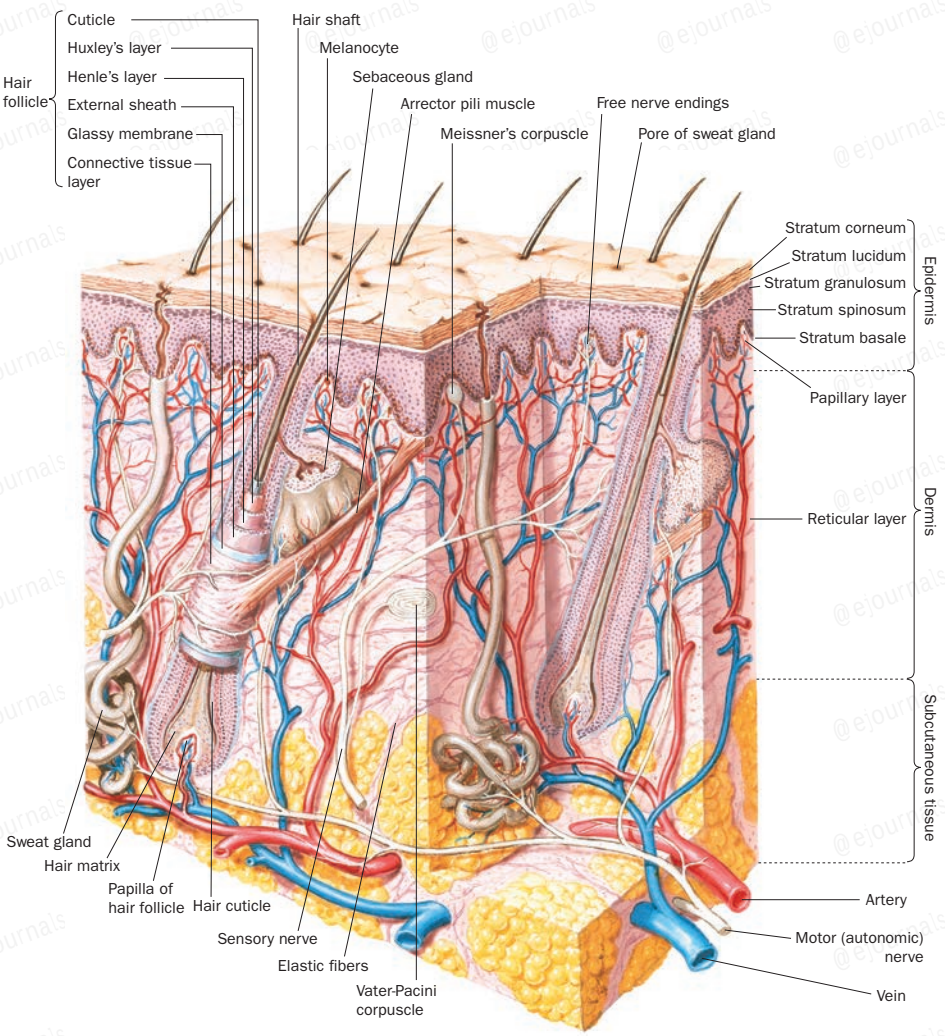

Fig. 1.1 Skin anatomy. (© 1967, CIBA Pharmaceutical Company, Division of CIBA-GEIGY Corporation. Reprinted with permission from Clinical Symposia. Illustrated by Frank H. Netter, MD. All rights reserved.)

Maintaining the Skin Barrier

- The skin assists in fluid homeostasis and protects against infections, toxins, and harmful effects of ultraviolet radiation.
- The outermost layer of the epidermis, the stratum corneum, provides this protection through an impermeable barrier made up of fatty acids, cholesterol, and ceramides cemented between tightly knit, protein-rich cornified cells.
- Keratinocytes serve skin barrier functions by contributing to the physical barrier as well as to the skin's innate immune defense (e.g., antimicrobial peptides, cytokines) and adaptive immune response.
- One goal of topical or systemic dermatologic therapy is to restore and maintain the essential functions of the skin barrier.

Skin Cleansing

- For most individuals, full-body daily bathing is not necessary for healthy skin.
- Patients should use mild soaps and cleansers, such as Cetaphil, Dove, Keri, Oil of Olay, or CeraVe, and should avoid excessive use of exfoliating scrubs, washcloths, and brushes.
- Soaps with fragrances and antibacterial agents can be irritating.
- Patients should bathe with tepid water and avoid washing with very hot water.

Skin Bathing and Soaking

- Bleach baths (¼–½ cup bleach added to half to full adult bath) are antimicrobial and anti-inflammatory and are useful for patients with infected eruptions, such as atopic dermatitis and stasis dermatitis. Bathe for 10 to 20 minutes twice weekly to daily. Skin should be moisturized after bathing.
- Aluminum acetate solution (e.g., Dumboro) and vinegar compresses soothe the skin when used for acute eczema and allergic contact dermatitis.
- Avoid bubble baths and fragranced bath oils because they can cause skin irritation and allergy.
- When bathing children, use soaps and shampoos at the end of the bath to minimize skin dryness.
- Apply moisturizers immediately after bathing and drying to trap in moisture.

Skin Moisturization

- A moisturizer is a compound that serves five principal functions: repairs the skin barrier, maintains skin integrity and appearance, reduces transepidermal water loss, restores the lipid barrier's ability to hold and redistribute water, and reduces skin inflammation.
- Occlusive moisturizers, such as petrolatum, act by preventing water loss from the skin. Lanolin, mineral oil, and silicones (e.g., dimethicone) are other occlusive moisturizers.
- Humectants, such as glycerin and hyaluronic acid, function by increasing absorption of water from the air to the epidermis.
- Emollient creams and lotions soften and smooth the skin and thereby improve the skin appearance.
- Immediately after washing, the skin should be patted dry and a moisturizer applied.
- Pure petrolatum is thought to be the least irritating moisturizer.
- Thick emollients, such as petrolatum, feel "greasy" and can block follicular and eccrine openings, producing acne and miliaria in rare cases.
- Lotions spread easily on the skin, but are not as effective in preventing water loss and skin protection as petrolatum and heavier creams.
- In some patients, preservatives (e.g., isothiazolinone) in creams and lotions cause skin irritation and allergic contact dermatitis.
- Patients with sensitive skin should apply lotions free of dyes and fragrances.
- Unscented soaps and moisturizers can contain masking fragrances, producing skin allergy.
- Many creams and lotions have "antiaging" additives, such as vitamins A, C, and E, but their efficacy is not proved.
- Sunscreens are added to many creams and lotions to slow skin aging.
- Avoid applying moisturizers with sun protection factor at night.

- Keratolytic emollients containing glycolic acids (lactic acid, salicylic acid) and urea are useful to gently exfoliate the skin.
- Sarna (camphor and menthol) and Pramosone (pramoxine and hydrocortisone) are examples of lotions with additives to decrease itch.
- Moisturizers decrease skin inflammation through barrier-enhancing properties.
- Atopiclair (2% glycyrrhetinic acid and shea butter), MimyX (*N*-palmitoylethanolamine), and EpiCeram (3:1:1 ratio of ceramides, cholesterol, and free fatty acids) are nonsteroidal creams able to improve inflammatory skin conditions, such as atopic dermatitis.
- Eletone is 70% oil in 30% water produced with "reverse emulsion" technology, affording the physiologic benefits of an ointment with the consistency of a cream.
- Promiseb and Loutrex are moisturizers with anti-inflammatory and antifungal properties that have been shown to improve inflammatory conditions, such as seborrheic dermatitis.
- Patients should check with their physician for specific skin care recommendations.

Examples of Lubricating Creams and Lotions

In addition to those named here, many other effective products are available.

Thicker Creams and Ointments

- Neutrogena Norwegian Hand Formula
- Theraplex Eczema Therapy
- Mustela Lipid-Replenishing Balm
- Vaseline petroleum jelly
- Aquaphor ointment
- Eucerin cream
- Hydrolatum

Lighter Creams

- Acid Mantle
- Cetaphil cream (many formulations)
- DML cream
- Moisturel cream
- Nutraplus cream
- Aveeno Eczema Therapy
- CeraVe cream
- Vanicream Moisturizing skin cream

Lighter Lotions

- Cetaphil lotion
- DML lotion
- Nutraderm lotion
- Curel lotion
- Aveeno lotion
- CeraVe lotion
- Vanicream Lite lotion

Topical Formulations

- Two principal factors must be considered when choosing a topical medication: the active drug and the drug delivery system or vehicle.
- For any given topical drug to be effective, it must be administered in an adequate concentration in a vehicle that effectively delivers the active ingredient into the skin.
- Vehicles not only assist in drug delivery but also have therapeutic properties.
- Ointments are greasy emulsions (70% oil in 30% water) that help deliver medications to dry skin. Ointments increase the potency of a compound compared with the cream formulations (e.g., Elocon ointment is more potent than Elocon cream).
- Creams are oil-in-water emulsions (50% oil in 50% water). They can be cooling and are not as occlusive as ointments.
- Pastes are ointments with 20% to 50% powder, such as zinc oxide or starch (e.g., Obtundia Calamine Cream). They are more drying than ointments and are less greasy. They help dry weeping eruptions, such as poison ivy.
- Solutions and lotions are clear or milky white liquids that evaporate on the skin and thus can be drying. They are effective in delivering drugs to hairy areas, such as the scalp, arms, and legs. Patients can experience stinging when used on open wet areas or on mucous membranes.
- Gels are clear and greaseless. They dry skin on contact, leaving a thin film. They are effective for treating acne and skin disease in hairy areas. Foams are similarly greaseless.
- Foams (e.g., Olux foam) are formed by trapping gas bubbles in a liquid or solid and are especially useful for delivering drugs to hair-bearing areas.

- Tapes (e.g., Cordran tape) can be impregnated with medication and are useful to treat localized areas, such as in psoriasis and warts.
- Powders are drying and are effective in moist intertriginous areas. They are vehicles for many antifungal agents.
- Like powder, water can dry weepy rashes, and it can be effective in removing scale and treating widespread skin disease (e.g., oatmeal bath, tar bath).

Topical Application and Dosing

- Medications should be gently massaged into the skin in one thin layer. Thicker applications do not increase skin penetration.
- One gram of cream covers an area 10 × 10 cm, and ointments spread slightly further.
- The fingertip unit (FTU) is another method to assess how much cream to dispense and apply. An FTU is the amount of ointment expressed from a tube with a 5-mm diameter nozzle and applied from the distal skin crease to the tip of the index finger. In an adult, 1 FTU weighs approximately 0.5 g. The number of FTUs required to cover specific body areas is illustrated in Appendix A.
- Dosing frequency varies with the medication, but most dermatology medications are applied once or twice per day.
- The ability of a medication to penetrate the skin varies according to the anatomic site (mucous membranes > scrotum > eyelids > face > torso > extremities > palms and soles).
- Conditions producing skin breakdown allow increased drug penetration. As the epidermal barrier function improves, less percutaneous absorption occurs.
- Medications placed under occlusive dressings or body suits are more readily absorbed into the skin.

Wet Dressings

- Wet dressings or compresses are a valuable aid in the treatment of exudative (wet) skin diseases.

1. Obtain a clean, soft cloth, such as bed sheeting or shirt material. The cloth need not be new or sterilized.
2. Fold the cloth and cut to fit an area slightly larger than the area to be treated.
3. Wet the folded dressings by immersing them in the solution, and wring them out to the point of sopping wet (neither running nor just damp).
4. Place the wet dressings on the affected area. Do not pour solution on a wet dressing to keep it wet because this practice increases the concentration of the solution and may cause irritation. Remove the dressing and replace it with a new one.
5. Leave the dressings in place for 30 minutes. Dressings may be used two to four times a day or continuously. Discontinue the use of wet dressings when the skin becomes dry. Excessive drying causes fissures.

- The temperature of the compress solution should be cool when an anti-inflammatory effect is desired and tepid when the purpose is to débride an infected, crusted lesion.
- A wet dressing should not be covered with a towel or plastic. A towel and plastic wrap, inhibit evaporation, promote maceration, and increase skin temperature, which facilitates bacterial growth.

Benefits of Wet Dressings

- Inflammation suppression—the evaporative cooling causes the constriction of superficial vessels, thereby decreasing erythema and the production of serum. Wet dressings soothe acute inflammatory processes, such as acute poison ivy.
- Wound débridement—the dressing macerates vesicles and crust, helping débride these materials when the dressing is removed.
- Drying—repeated cycles of wetting and drying promote drying of weeping wet lesions.

Pediatric Considerations

- Infants have a markedly increased body surface area compared with body mass, placing them at risk for systemic side effects and toxicity from topically applied medications.
- Premature infants have compromised epidermal permeability barriers, allowing percutaneous absorption and systemic toxicity from medications and even harmless substances, such as soaps and cleaning solutions.
- Infants under warming lights and postmature infants often have dry, flaky skin with fissures and benefit from application of bland ointments and creams.
- School-aged children often overclean the back of their hands, resulting in dry, cracked skin.

Fig. 1.2 Application of wet compresses soothes the skin and is effective in treating weeping inflammatory rashes.

Topical Corticosteroids

Description

- Hydrocortisone was first introduced in 1952, and since then, topical corticosteroids have been the principal medications used to treat inflammatory dermatosis. Over time, they have been proved safe and effective when used properly. In dermatology, topical corticosteroids are used for their anti-inflammatory properties.

Generic Versus Brand Names

- Many generic topical corticosteroid formulations are available and provide substantial financial savings for patients.
- Despite these savings, generic formulations can differ significantly from their brand-name counterparts with respect to their anti-inflammatory potency and preservative content.

Corticosteroid Potency: Groups I to VII

- Topical corticosteroids are organized in seven groups, based on their anti-inflammatory activity (group I is the strongest; group VII is the weakest; see inside back cover for group listings).
- Throughout the book, topical corticosteroids are referred to by group number.

Choosing the Appropriate Strength

- The success or failure of therapy depends largely on selecting a topical corticosteroid of the correct strength.
- A few essential factors to consider include diagnosis, location, age, and financial resources of the patient.
- Certain rashes, such as nummular eczema and discoid lupus erythematosus, require group I or II corticosteroids for adequate control. Seborrheic dermatitis is responsive to groups V to VII corticosteroids.
- Dermatitis on the eyelids should be treated with groups V to VII corticosteroids. Palms and soles require groups I to III corticosteroids because the thick skin obstructs penetration and lessens efficacy.
- Patients who do not show adequate response after 2 weeks of therapy should be re-evaluated.
- By convention, topical corticosteroids are firmly massaged into the skin twice daily, although some formulations only require once-daily application.
- Concentrations reflect relative strength for a particular corticosteroid (triamcinolone 0.025%, 0.05%, 0.1%) and cannot be used to compare strengths between corticosteroids. For example, clobetasol propionate 0.05% is much more potent than hydrocortisone 1%.
- Some corticosteroids are referred to as *fluorinated* because a fluorine atom has been added to increase potency.

Prescribing Topical Corticosteroids

Dosing Schedules

- These are general guidelines; specific instructions and limitations must be established for each patient.

Superpotent Topical Corticosteroids (Group I)

- Patients should not use more than 45 to 60 g of cream or ointment per week.
- Cyclic dosing, such as corticosteroid application for 2 weeks, followed by 1 week of rest, can limit side effects.
- Patients must be prescribed limited amounts of these superpotent corticosteroids and have close monitoring.
- Difficult-to-treat inflammatory diseases, such as plaque psoriasis and hand eczema, respond most effectively when a group I topical corticosteroid is applied twice a day for 2 weeks, followed by 1 week of rest. This schedule is repeated until the condition is well controlled.

Groups II to VII Topical Corticosteroids

- Groups II to VII topical corticosteroids should be applied twice each day.
- Adequate response should be seen in 2 to 6 weeks.
- Prescribing a weak group VII topical corticosteroid (hydrocortisone) for an intense inflammatory condition is a common mistake.

Methods of Application (Simple and Occlusive)

Simple

- A simple application refers to massaging a topical corticosteroid thinly into the skin without the aid of an occlusivedressing.
- Washing is not necessary before each application.
- Different skin surfaces vary in their ability to absorb topical corticosteroids.
- Eyelid dermatitis responds quickly to group VI or VII steroids. Higher potency corticosteroids should be avoided in this area.
- The skin on the palms and soles is thick, requiring groups I to III corticosteroids.
- Intertriginous areas (e.g., axilla, groin, perineum, and the inframammary region) respond quickly to groups V to VII corticosteroids because the moisture and occlusion increase percutaneous absorption.
- Topical corticosteroids are absorbed readily in inflamed skin, resulting in a rapid initial response.

Occlusive

- Occlusive dressings (e.g., Saran Wrap) hydrate the stratum corneum and allow for enhanced corticosteroid absorption and thus for use of lower strength corticosteroids.
- Lengthy application of an occlusive dressing can produce superficial skin infection (usually *Staphylococcus aureus*) and inflamed hair follicles. If pustules develop, topical (e.g., mupirocin or retapamulin) or systemic (e.g., cephalexin, trimethoprim-sulfamethoxazole), antistaphylococcal antibiotics should be administered.
- Occlusive dressings can be used during the day for periods of up to 2 hours, or for up to 8 hours during sleep. Simple applications can be alternated with applications assisted by an occlusive dressing.

Method of Occlusion

- The area should be cleaned with mild soap and water. Antibacterial soaps are unnecessary.
- The topical corticosteroid is gently rubbed into the lesions, and the entire area is

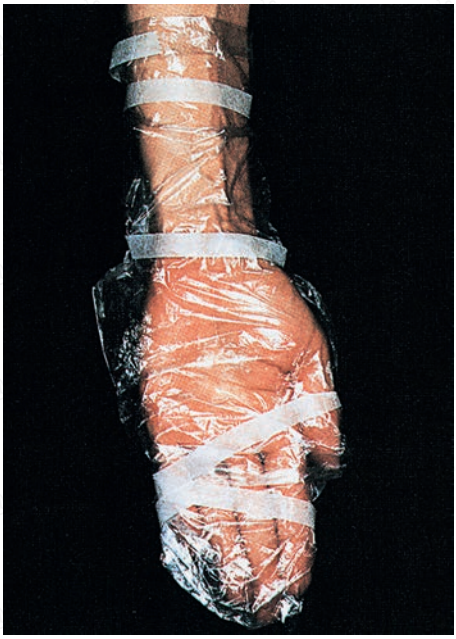

Fig. 1.3 Occlusion of the hand. A plastic bag is pulled on and pressed against the skin to expel air. Tape is wound snugly around the bag.

Fig. 1.4 Occlusion of the arm. A plastic sheet (e.g., Saran Wrap) is wound around the extremity and secured at both ends with tape. A plastic bag with the bottom cut out may be used as a sleeve and held in place with tape or an Ace bandage.

Fig. 1.5 Sauna suits may be used to help moisturize the skin and increase effectiveness of topical corticosteroids. They can be purchased on the Internet or from major retail stores.

covered with plastic (e.g., Saran Wrap, Handi-Wrap, plastic bags, vinyl gloves, or vinyl exercise suits).

- The dressing is secured with tape so that it is close to the skin and the ends are sealed. An airtight dressing is not necessary. The plastic may be held in place with an Ace bandage or a sock.
- The best results are obtained when the dressing remains in place for at least 2 hours. Many patients find that bedtime is the most convenient time to wear an occlusive dressing.
- More medicine is applied shortly after the dressing is removed and while the skin is still moist.
- Vinyl exercise suits are effective to occlude large body surface areas.

Systemic Absorption

- With proper use of corticosteroids, systemic effects are rare.

Fig. 1.6 Steroid atrophy. Long-term application of clobetasol, a group I topical steroid, caused dermal atrophy and skin fragility. Bleeding and skin tearing occurred with the slightest trauma.

- Persistent, unsupervised use of topical corticosteroids over wide areas can result in significant systemic absorption.

Steroid–Antibiotic Mixtures

- Some products contain a combination of antibiotics and corticosteroids.
- Most corticosteroid-responsive skin diseases can be managed successfully without topical antibiotics, limiting the usefulness of these products.
- Neomycin is a common cause of allergic contact dermatitis and should be avoided.
- Antifungal–corticosteroid combinations (Mycolog, Lotrisone) are expensive and have limited uses. The topical corticosteroid betamethasone diproprionate (found in Lotrisone) is too strong for intertriginous areas and can cause permanent striae.

Adverse Reactions

- Topical corticosteroids have the following potential side effects:
  - Allergic contact dermatitis
  - Burning, itching, irritation, dryness (largely due to the vehicle)
  - Hypertrichosis
  - Hypopigmentation
  - Miliaria and folliculitis
  - Skin breakdown
  - Glaucoma, cataracts
  - Rebound phenomenon (e.g., psoriasis becomes worse after treatment is stopped)
  - Rosacea, perioral dermatitis, acne
  - Skin atrophy with telangiectasia, stellate pseudoscars (arms), purpura, striae

- Skin blanching from acute vasoconstriction
- Systemic absorption
- Tinea incognito, impetigo incognito, scabies incognito

Fig. 1.7 Striae. Long-term application of a group V topical steroid to the axillae produced striae. This side effect is irreversible.

Pediatric Considerations

- Topical corticosteroids have been used in children for more than 40 years and have a proven track record for safety when used correctly.
- Many parents have concerns about topical steroids. Parents should be educated about potential side effects and shown how to apply topical steroids correctly.
- Infants are more susceptible to systemic side effects because of their increased ratio of body surface to weight. Systemic side effects, such as hypothalamic–pituitary axis suppression, can occur with long-term use or when the skin barrier is compromised (acute dermatitis, premature infants).

Fig. 1.8 Steroid rosacea. Numerous papules and pustules appeared on the face after stopping application of a group II topical steroid. The topical steroid had been applied daily for 12 weeks.

Fig. 1.9 Atrophy and telangiectasia after continual use of a group II topical steroid for 6 months. The atrophy may improve after the topical steroid is discontinued, but the telangiectasia often persists.

Fig. 1.10 Steroid atrophy. Atophy may occur on the palms and soles with long term use of superpotent topical steroids. Notice the porcelain white atrophy in the arch of the foot after 3 months of application of clobetosol.

Fig. 1.11 Striae of the groin after long-term use of group V topical steroids for pruritus. These changes are irreversible.

Fig. 1.12 Steroid atrophy. Long-term daily application of clobetasol, a group I topical steroid, caused epidermal and dermal atrophy with telangiectasia. Veins can be seen through the thinned skin.

Fig. 1.13 Application of topical corticosteroids to the face may result in rosacea, as seen in this patient.

Fig. 1.14 Typical presentation of tinea of the groin before treatment. A fungal infection of this type typically has a sharp, scaly border and shows little tendency to spread.

Fig. 1.15 Tinea incognito. Bizarre pattern of widespread inflammation created by applying a group II topical steroid twice daily for 3 weeks. The facial eruption is similar in appearance to the groin rash in Fig. 1.14. A potassium hydroxide preparation showed numerous fungi.

2 Eczema

Kathryn A. Zug

Acute Eczematous Inflammation

Description

- Acute eczematous inflammation is characterized clinically by erythema, edema, and vesiculation. Weeping or oozing of acute lesions is typical. Pruritus is often severe.

History

- There are multiple causes of acute eczema. They include allergic contact hypersensitivity to specific plant allergens, such as poison ivy, poison oak, or poison sumac, and many other allergens.
- Nickel, topical medicaments (e.g., bacitracin, neomycin, and benzocaine), fragrances, preservatives in personal care products, occupation-associated sources, and rubber additives are also common causes of acute eczematous inflammation. Irritant dermatitis is common after repeated water, solvent, or detergent exposure and predisposes to contact allergy.
- In an "id reaction," acute eczema with vesicles occurs at a distant site (e.g., the hands) from an active fungal infection (e.g., the feet).
- Stasis dermatitis, scabies, irritant reactions, and dyshidrotic and atopic eczema may present as an acute eczematous inflammation.

Skin Findings

- Findings include erythema, edema, vesiculation, and weeping. Inflammation can be moderate to intense. Tiny, clear, fluid-filled vesicles are seen on the skin surface. Bullae may develop.

Laboratory

- Patch testing to evaluate for delayed-type hypersensitivity should be considered if the distribution suggests a contact exposure, if the problem is recurrent or refractory to therapy, or if there is known occupational, hobby, or other exposure to cutaneous allergens.
- Consider mineral oil preparation to evaluate for scabies, especially in eczema of new or recent onset.
- Consider scraping scale for potassium hydroxide examination to evaluate for dermatophyte fungus infection. Blood tests are almost never helpful in the evaluation of acute eczema.

Course and Prognosis

- If the provoking factors can be avoided, the eruption improves over 7 to 10 days, with clearing usually by 3 weeks. Recurrence may indicate allergen re-exposure.
- Excoriation predisposes to infection and causes serum, crust, and purulent material to accumulate. Excoriation can result in secondary staphylococcal infection and in aggravation and prolongation of the dermatitis.

Management

- Cool, wet dressings and topical steroid creams allow vasoconstriction and suppress inflammation and itching. A clean cloth is soaked in cool water or Burow's solution and then placed on affected areas for 30 minutes. An appropriate topical steroid cream (group II or III) is then applied and rubbed in well.
- Oral corticosteroids are reserved for severe or generalized acute eczema. The dosage is approximately 0.5 to 1 mg/kg/day initially, tapering over 3 weeks. Too short a course may result in recurrence and rebound of the dermatitis.
- Oral antihistamines, such as diphenhydramine (Benadryl) and hydroxyzine (Atarax), can relieve itching, and their sedative effect may promote better sleep.

Fig. 2.1 Acute eczema with vesicles, erythema, edema, and weeping.

Fig. 2.2 Acute eczematous inflammation.

- If secondary infection is suspected, an anti–*Staphylococcus aureus* antibiotic (e.g., cephalexin, dicloxacillin) is administered for 10 to 14 days.

Pearls

- Acute eczema may be confused with acute infections, such as cellulitis; the often marked itching associated with acute eczema should help distinguish them.
- Repeated bouts of acute eczema on the face, exposed hands, or arms suggest a contact allergy that should be evaluated by patch testing. Scabies should be considered in new-onset eczema.
- Remove all the patient's topical medications (lotions, topical over-the-counter medicaments, anti-itch preparations) and treat with topical steroids only, or with bland emollients—keep the skin care and exposures minimal and simple.
- Elevation of the legs, if they are affected, is helpful in decreasing dependent edema and dermatitis.

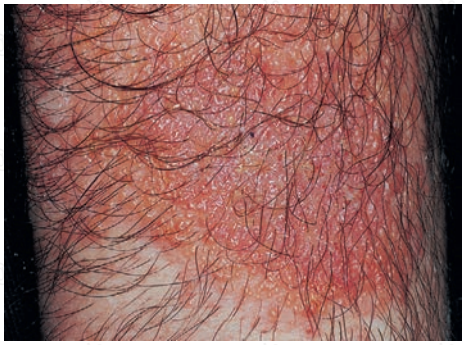

Fig. 2.3 Acute eczema. Pruritic vesicles are the hallmark.

Fig. 2.4 Acute eczematous inflammation. Vesicles and intense itching are the hallmark of acute eczema. This patient was allergic to rubber allergens in shoes.

Fig. 2.5 Acute eczema. Poison ivy may cause intense acute eczematous inflammation. Vesicles and blisters form on a red base. The blisters may coalesce and become very large. The itching is unbearable and is best controlled with cold wet dressings.

Fig. 2.6 Vesicles are characteristic of the acute phase of eczematous inflammation. Itching is often intense.

Rhus Dermatitis (Poison Ivy, Poison Oak, Poison Sumac)

Description

- Poison ivy, poison oak, and poison sumac (plants of the Anacardiaceae family) and *Toxicodendron* species are the most common causes of allergic contact dermatitis in the United States; this problematic prototype of contact dermatitis is rarely reported in Europe, although related plants grow in Southeast Asia, Central America, and South America.
- Oleoresin (lipid-soluble portion) contains a mixture of highly allergenic catechol chemicals called *urushiols*, a term derived from the Japanese word for sap, *urushi*.

History

- Contact with the plant's leaf, stem, or root, even in autumn and winter, results in a pruritic bullous eruption within 8 to 72 hours of exposure in a previously sensitized individual and within 12 to 21 days in an individual who has not yet been sensitized (primary sensitization).
- Primary sensitization can result from exposure to the allergenic plant. This process requires an intact immune system. After an individual has become allergic (sensitized), repeat exposure will cause the rash to occur more promptly (a process called *elicitation*).
- About half of American adults develop the rash if they are exposed; 30% to 40% require prolonged exposure to produce the dermatitis.
- About 10% to 15% of Americans do not become sensitized (allergic).

Skin Findings

- Clinical findings vary with the quantity of oleoresin that contacts the skin, the pattern of contact, individual susceptibility, and regional variations in skin reactivity.
- Findings include pruritic, edematous, linear erythematous streaks, usually with vesicles and large bullae on exposed skin.
- Airborne particulate matter from burning the plant can result in intense, pruritic facial erythema and marked edema; the eyelids can be dramatically swollen.
- Trauma to the skin from the plant may leave a temporary black mark on the skin—a clue to exposure and a result of dried and oxidized urushiol allergen.

Course and Prognosis

- The itchy eruption lasts from 10 days to as long as 3 weeks.
- Short courses of oral corticosteroids (e.g., dose packs) are inadequate and may result in a rebound phenomenon with prompt blistering when discontinued.
- The rash resolves completely without scarring.
- Impetigo or cellulitis may occur from scratching and secondary bacterial infection (usually *S. aureus*).
- Short-term disability and time lost from work are significant occupational problems associated with this contact dermatitis, especially among firefighters, foresters, landscapers, and outdoor workers.

Discussion

- Poison ivy is not spread by blister fluid and is not spread from person to person.
- The allergenic oleoresin can be spread by contaminated clothing, garden tools, or animals.
- Cross-reacting allergens from other plants of the Anacardiaceae family include mango peel, the oil of raw cashew nut shells, Japanese lacquer, and ginkgo fruit pulp. Individuals sensitized to poison ivy may also react after exposure to these related plants.
- Poison ivy grows as a shrub or climbing vine. In the United States, Eastern poison oak is typically found in the Southeast, whereas Western poison oak grows typically on the West Coast, in the form of a small shrub or tree. Poison sumac prefers a moist location and is common in peat bogs and wetlands of the eastern United States and southeastern Canada.

Management

- The skin should be washed with soap to inactivate and remove allergic oleoresin, thereby preventing further skin penetration and contamination. Washing is most

Fig. 2.7 Poison ivy dermatitis. Classic presentation of linear vesicles in streaks suggests plant dermatitis.

effective if done within 15 minutes of exposure.

- Exposed clothing and tools should be cleansed with soapy water.
- Short, cool tub baths, with or without colloidal oatmeal (Aveeno), are soothing for itching and swelling.
- Calamine lotion controls itching, but prolonged use can lead to excessive drying.
- Oral antihistamines (hydroxyzine and diphenhydramine) may control itching. They are sedating and may be best used at night to reduce nighttime scratching and promote rest, thus offering relief from the stress of intense itch, which often interferes with sleep.
- Cool, wet dressings made with tap water or Burow's solution are highly effective during the acute blistering stage. They are applied for 15 to 30 minutes several times a day for 1 to 4 days until blistering and severe itching are controlled. Cool, wet tap-water dressings are very useful for severe facial or eyelid edema.
- A medium-potency topical steroid (groups II–V) should be generously applied after the wet dressing. If the periorbital skin is involved, a weaker topical steroid (groups VI–VII) is advised for a specified limited duration (twice daily for 7 days).
- The immunomodulatory topical therapies, pimecrolimus (Elidel) and tacrolimus (Protopic), are not advised for acute allergic contact dermatitis to poison ivy, given their cost, the amount often required, and delay of efficacy compared with topical steroids.
- A course of oral corticosteroids for severe, widespread inflammation is started at 0.5 to 1 mg/kg/day and is slowly tapered over 3 weeks.
- A barrier cream, IvyBlock, contains quaternium-18 bentonite that can be successful in preventing the dermatitis or reducing the severity of reactions. However, it is essential that it be applied at least 15 minutes before anticipated exposure.
- Poison ivy oleoresin in capsules and an injectable form for hyposensitization have been removed from the market as a result of side effects and incomplete efficacy. There are no means available currently for desensitization to poison ivy.

Fig. 2.8 Edema, erosions from large bullae, and vesicles on this limb affected by a severe contact allergy to poison ivy. Itch rather than pain fits with allergy and not infection.

Fig. 2.9 Poison ivy dermatitis. Intense erythema, vesicles, and itching are intolerable. Cold tap-water compresses are soothing. Severe poison ivy dermatitis may require systemic treatment.

Fig. 2.10 Poison ivy dermatitis occurs at site of contact with the allergenic oil of the plant. Plant leaf used as toilet wipe resulted in rash in gluteal cleft. Spread of oil from hands to genital skin is not uncommon, and the result is very uncomfortable.

Pearls

- The classic presentation of poisonous plant contact dermatitis is variably sized vesicles and bullae appearing in a linear distribution on exposed skin.
- Generally, repeated exposure over short periods of time (i.e., the summer months) results in increasingly severe bouts of the dermatitis.
- Oral ingestion of raw or incompletely roasted cashews can cause an internal–external reaction—a sudden erythematous pruritic dermatitis in a characteristic distribution on the buttocks, upper inner thighs, and axillary vault in individuals sensitized to urushiol.

Fig. 2.11 Poison ivy plant. Note the leaves of three and small berries.

- Poison ivy, poison oak, or poison sumac can involve wide areas. The decision to use oral or topical steroids depends on the severity of the symptoms, age of the patient, and potential for short-term adverse reactions anticipated through review of the medical history.
- Short courses of low-dose systemic corticosteroids are inadequate treatment for severe, generalized cases of poison ivy.

Fig. 2.12 Poison ivy with severe, intense, acute eczematous inflammation and large confluent blisters. Many blisters have ruptured. The serum that leaks onto the skin does not spread poison ivy. Cool wet compresses applied for 30 minutes several times a day help to control the inflammation.

Fig. 2.13 Large bulla of poison ivy can become blood filled.

Subacute Eczematous Inflammation (Subacute Eczema)

Description

- This eczematous inflammation consists of itchy, red, and scaling patches, papules, and plaques in various configurations.

History

- This subacute condition may evolve from acute (vesicular) eczema.
- This is the most common clinical manifestation of atopic dermatitis. It may also represent contact allergy.
- Patients complain of dermatitis that has been present longer than 1 week.
- Itching is variable; it can be moderate to severe or rather mild.
- The condition resolves without scarring when provoking or contributing aggravating factors are removed. It may require treatment to resolve.
- Excoriation and repeated exposure to aggravating conditions (water, detergents, irritants, or other common irritants or allergens) convert this condition to a chronic process.

Skin Findings

- Erythema and scaling occur in various patterns.
- Often there are indistinct borders.
- Redness may be faint or intense.

Etiology and Clinical Presentation

- Contact allergy, contact irritation, atopic dermatitis, scabies, stasis dermatitis, nummular eczema, fingertip eczema, and fungal infections may present as subacute eczema.
- If there is not a strong atopic history, search for new cutaneous irritant or allergen exposures. Stress can aggravate and contribute to this problem but is not a common sole cause.

Treatment

Steroids and Other Nonsteroid Topical Prescription Therapies

- Groups II to V steroid creams twice a day with or without plastic occlusion are administered. Occlusion hastens resolution while increasing absorption of topical steroid. Duration of occlusion should be specified (2–8 hours) and limited (3–10 days).

Fig. 2.14 Subacute eczema of the ear with erythema, scaling, and crusting.

Fig. 2.15 Erythema and scaling with indistinct borders are characteristic. Vesicles may never appear. This is often the initial presentation in the winter in atopic patients.

- Steroid ointments can be applied twice a day without occlusion.
- Nonsteroid topical immune modulators tacrolimus (Protopic ointment 0.1, 0.03%) and pimecrolimus (Elidel cream 1%) can be applied twice daily to affected skin and are especially useful in subacute eczema of the face or periorbital eyelid skin. They may initially cause some stinging or burning of the skin, which subsides in a few days. These therapies are useful for chronic management of subacute eczema in atopic patients.
- Tar ointments and creams (many over-the-counter preparations) provide an alternative for steroid-resistant lesions and are moderately effective in some patients.
- Wet dressings should be avoided because they cause excessive dryness.

Moisturizers

- Moisturizers are an essential part of daily therapy.
- Moisturizers work best when applied a few hours after topical steroids.
- Application should continue for days or weeks after the inflammation has cleared.
- Frequent application is encouraged.
- Moisturizers are most effective when rubbed in well and applied directly after the skin is patted dry following a shower.
- Creams with simple formulations lacking the most common allergy-associated ingredients (e.g., Vanicream, Aveeno, Cetaphil, DML, and CeraVe) are better than lotions. Plain petroleum jelly is an excellent moisturizer and has the advantage of being plain, without allergenic additives or irritating ingredients. Greasiness limits patient acceptability. Coconut oil is also an excellent moisturizer with low sensitization risk.
- Infrequent washing with bar-type mild soap (e.g., Dove, Cetaphil, Keri, Purpose, and Basis) is also helpful.

Antibiotics

- Antibiotics (e.g., cephalexin, dicloxacillin) are used for secondary bacterial infections (usually *S. aureus*). Culture may be necessary to evaluate for methicillin-resistant *S. aureus.*

Fig. 2.16 Subacute eczematous inflammation. The configuration of subacute inflammation varies. Plaques may be patchy or confluent, round or diffuse.

Fig. 2.17 Subacute eczematous inflammation. This plaque is dense and covered with scale. The borders are somewhat distinct. Differentiation from psoriasis in this case would be difficult. The history and types of plaques in other areas may be needed to confirm a diagnosis.

Fig. 2.18 Subacute eczematous inflammation. Patchy, ill-defined eczema is seen on the arm and trunk. Individual crusted papules suggest the possibility of scabies in the differential diagnosis.

Fig. 2.19 Subacute eczematous inflammation. A subacute dermatitis consisting of erythematous papules, patchy erythema, and crusting. This location is more typical for metal contact allergy due to nickel. Often the dermatitis spreads elsewhere, a process referred to as *autoeczematization*.

Fig. 2.20 Subacute eczema. Note the fissuring on the surface, the cracked appearance and scaling, some surface crust, and erythema.

Fig. 2.21 Subacute eczema of the dorsum of the hands is seen here with weeping, crusting, vesiculation, and erythema.

Fig. 2.22 Subacute eczematous dermatitis of the hand. Fissuring, scaling, and dull pink erythema in ill-defined patches. This is a typical appearance of irritant dermatitis from repeated hand washing.

Pearls

- Subacute eczema is a clinical manifestation of ongoing inflammation. Attention to cutaneous exposures of irritants, allergens, and the patient's overall skin care regimen is vital to addressing causes and aggravating factors.
- Consider a potassium hydroxide examination of scale to rule out dermatophyte infection.
- Ask about the patient's occupation, topical product use, house duties, and hobbies because they may contribute to ongoing skin irritation or risk for developing contact allergy. Vinyl gloves serve as a useful protective barrier if repeated exposure to water, irritants, or allergens is occurring. Vinyl gloves are a good choice because they do not contain common rubber-related allergens (gloves can be ordered online from http://www.allerderm.com).

Fig. 2.23 Subacute eczematous inflammation is characterized by erythema and scaling. There are no blisters. An allergic reaction to neomycin ointment produced this eruption.

Fig. 2.24 Subacute eczema of the fingers is common in people who have repeated exposure to moisture. New mothers who wash and clean are at a high risk for irritant eczema.

Fig. 2.25 Subacute eczema with indistinct borders, erythema, scaling, and pruritus. This is the appearance of a long-standing contact allergy. Patch testing should be considered.

Fig. 2.26 The forearm of a patient with generalized atopic dermatitis. Subacute eczema is characterized by ill-defined, coalescing papules, erosions, crusting, scaling, and early lichenification.

Fig. 2.27 Subacute eczema. Eczema of the areola and nipple is not uncommon in patients with atopic dermatitis. However, refractory eczema at this site when unilateral should be excised for biopsy because Paget's disease is in the differential diagnosis.

Fig. 2.28 Eczema resembling psoriasis. Repeated vesiculation within this patch leads to subacute eczema.

Chronic Eczematous Inflammation

Description

- Affected skin is inflamed, red, scaling, and thickened (lichenified).

History

- There is moderate to intense, prolonged itching.
- Scratching and rubbing become habitual and may be done subconsciously.
- The disease becomes self-perpetuating. It often is frustrating and emotionally exhausting for the patient.
- Scratching leads to thick skin, which itches even more.

Skin Findings

- Intense itching can lead to excoriations.
- Inflamed, itchy skin thickens, and surface skin markings become more prominent.
- Thick plaques with deep parallel skin markings appear (lichenification).
- Sites commonly involved are those easily reached or creased areas.
- Common locations are the back of the neck, popliteal fossae, ankles, eyelids, and anogenital skin.
- Hyperpigmentation or hypopigmentation can occur on affected skin.

Etiology and Clinical Presentation

- Atopic dermatitis, chronic allergic or irritant contact dermatitis, habitual scratching, scabies, lichen simplex chronicus, chapped and fissured feet, nummular eczema, asteatotic eczema, fingertip eczema, and hyperkeratotic eczema are possible etiologies. Cutaneous T-cell lymphoma should be considered and may need to be excluded by multiple biopsies and molecular studies.
- The evolution of this process is the result of a chronic process.

Treatment

- Chronic eczematous inflammation is often resistant to treatment; the key to success is breaking the itch–scratch cycle through treatment and removal of the cause or sources of aggravation, including delayed type hypersensitivity allergens which can be identified by patch testing.
- A cool, wet dressing on the affected skin for 20 minutes will help soothe and diminish itch; it can be very helpful for the nighttime itch urge. It should be followed by emollient use or topical steroid application.

Fig. 2.29 Weeks of scratching and rubbing with the heel had caused skin thickening. The chronically inflamed and excoriated skin has become infected. Crust and purulent material cleared after a course of cefalexin 500 mg twice daily for 7 days.

Fig. 2.30 Chronic eczematous inflammation is characterized by dull pink erythema, thickening of the skin (lichenification), and scaling. Note the increased linear markings within this plaque.

Fig. 2.31 Chronic eczema of the dorsal fingers characterized by linear painful fissures, erythema, scaling, and swelling. Contact irritant versus contact allergic dermatitis should be considered, and patch testing should be done if patient does not get better with initial management.

Fig. 2.32 Chronic hand dermatitis characterized by erythema, fissuring, scaling, and thickened, retained scale (hyperkeratosis). Contactants, both irritant and allergic, should be considered. Patch testing is indicated for recurrent disease.

Fig. 2.33 Subacute and chronic eczema of the eyelids. Fine scaling and erythema. This picture could represent changes of irritant, allergic, or atopic dermatitis.

Fig. 2.34 Chronic eczematous inflammation. Fissuring, erythema, and scaling are seen in the postauricular crease. Differential diagnosis includes contact allergy and atopic eczema.

Fig. 2.35 Classic chronic eczematous changes of lichenification, scaling, and erythema with a plaque on the side of the hand. Repeated scratching and rubbing causes skin thickening.

Fig. 2.36 Increased linear markings on the wrist of a patient with atopic dermatitis. The medial wrists are often affected in atopic dermatitis.

Topical Steroids

- Group I or II creams or ointments applied twice a day can be effective.
- Groups II to V steroids are used with plastic occlusion for 2 to 8 hours.
- Intralesional injections (e.g., Kenalog diluted to 2.5–5 mg/mL) are very effective; resistant plaques are reinjected at 3- to 4-week intervals. Atrophy is a possible adverse effect.
- Steroid-impregnated tape (e.g., Cordon tape) should be left on for 12 hours.

Fig. 2.37 Erythematous scaling patches and heavy crusting. Weeping is a feature of acute eczema. The heavy crust can signify a staphylococcal secondary infection within this eczematous hand dermatitis.

Systemic Therapy

- Steroid sparing agents including mycophenolate mofetil, azathioprine, methotrexate, and cyclosporine have all been used in the treatment of chronic eczema. Newly approved dupilumab is a major advance in therapy for chronic, severe eczema. It is administered every two weeks.

Pearls

- Chronic rubbing or scratching is at least part of the problem—address it and aim to diminish it.
- Ointments penetrate lichenified skin well and are generally more effective than creams on lichenified skin.
- Consider and evaluate for contact irritants and allergens. Patch test to evaluate for contact allergy. Simplify the skin regimen: mild soaps, bland emollients (petrolatum, Vanicream, CeraVe, or Cetaphil) only.
- Protopic ointment (tacrolimus) can be helpful for involved lichenified chronic eczema on the face.

Lichen Simplex Chronicus

Description

- A localized plaque of chronic eczematous inflammation is created by habitual rubbing and scratching.
- The affected skin is frequently located on the wrists, ankles, anogenital skin, and back of the neck.

History

- This condition is more common in adults but may be seen in atopic children.

Skin Findings

- Findings include a sharply demarcated, deeply violaceous colored or red scaly plaque with prominent skin lines (lichenification).
- Although this is a chronic eczematous disease, acute changes of vesiculation and weeping may result from sudden allergy to topical treatments.
- Moist scaling, serum, crust, and pustules signal secondary infection.
- Nodules, usually smaller than 1 cm and scattered randomly in the scalp, occur in patients who frequently pick at the scalp.
- The areas most commonly affected are conveniently reached; these areas include the outer portion of the lower legs, wrists and ankles, posterior neck, scalp, upper eyelids, the fold behind the ear, scrotum, vulva, and anal skin.

Laboratory

- A potassium hydroxide scraping should be considered to look for tinea. Tinea infection can mimic lichen simplex chronicus.
- A contact allergy may cause, lead to, or complicate lichen simplex chronicus. Patch testing to identify the role of allergens can be helpful.

Course and Prognosis

- A typical plaque stays localized and shows little tendency to enlarge with time. After established, the plaque does not usually increase in size.

Treatment

- Stress may play a role in some individuals and should be acknowledged and addressed.
- The patient should understand that the rash does not resolve until even minor scratching and rubbing are stopped. Education and patient behavior insight are critical.
- Scratching frequently takes place during sleep, and the affected area may have to be covered.
- Treatment consists of a 5-minute water soak followed by the application of a topical steroid with medium-to-high potency in an ointment base.
- The treatment of the anal area, genitalia, or fold behind the ear does not usually require the administration of potent topical steroids; rather, these areas should be treated with low-potency topical steroids in an ointment base.
- For scalp lesions, a group I or II steroid gel, such as fluocinonide (Lidex), or a solution, such as clobetasol (Cormax scalp solution) or betamethasone dipropionate lotion (Diprolene), is applied twice each day.
- Moist, secondarily infected areas respond to oral antibiotics and a topical steroid lotion.
- Grenz ray (superficial x-ray) therapy can be helpful but has limited availability.
- Nodules caused by picking at the scalp may be very resistant to treatment, requiring monthly intralesional injections with triamcinolone acetonide (Kenalog diluted to 2.5–5 mg/mL).

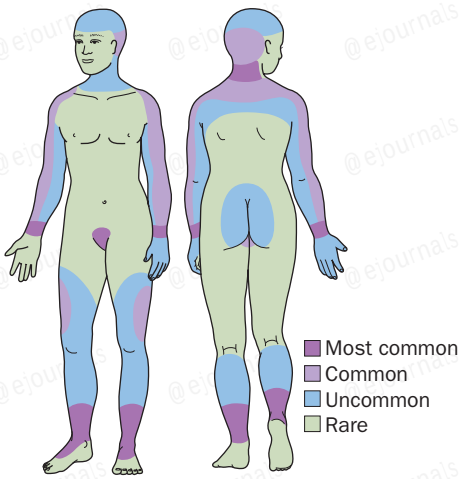

Fig. 2.38 Lichen simplex chronicus distribution diagram.

Fig. 2.39 A lesion of lichen simplex chronicus. Note the sharp demarcation of affected skin.

Fig. 2.40 Heme crusts, lichenified plaques, erythema, and scaling are features seen in this chronic foot dermatitis.

Fig. 2.41 Chronic eczematous dermatitis at the nape of the neck is common in patients with atopic dermatitis. This can be easily mistaken for psoriasis.

Discussion

- This condition was once referred to as *localized neurodermatitis*.
- The patient can derive great pleasure from scratching to relieve the inflamed site. Loss of pleasurable sensation or continued subconscious habitual scratching may explain why this eruption frequently recurs.
- Lichen simplex chronicus affecting the genitalia or anus can be a very chronic, difficult problem causing considerable distress and frustration.

Pearls

- The occipital scalp is possibly the most common target for anxiety-induced scratching. Very thick plaques may form

Fig. 2.42 Erythema, scaling, and crusting of the perianal skin. Contact allergy to ingredients, such as preservatives or fragrances in moist toilet paper (e.g., baby wipes), or allergens (e.g., fragrance or preservatives) may be causal or contributory.

that are difficult to manage, and sometimes they become infected.

- Although stress does not cause this condition, it most definitely contributes to aggravating and perpetuating it. Ask about stress, address the role it can play, and seek avenues for stress reduction.
- Nighttime itching can be diminished with this routine: oral antihistamines, such as diphenhydramine (Benadryl) or hydroxyzine (Atarax); followed by a 20-minute cold wet tap-water dressing; followed by application of a topical steroid to the affected skin.
- Consider patch testing for lichen simplex chronicus affecting the periorbital skin, the dorsal hands or feet, or the anogenital skin.
- Compliance is important to resolution of this problem. Take time and be specific in the explanation of your goals and treatment.

Box 2.1 Lichen Simplex Chronicus

Areas most commonly affected are listed in approximate order of frequency:

- Outer lower portion of lower leg
- Scrotum, vulva, anal area, and pubis
- Wrists and ankles
- Upper eyelids
- Back (lichen simplex nuchae) and side of neck
- Orifice of the ear
- Extensor forearms near elbow
- Fold behind the ear
- Scalp-picker's nodules

Fig. 2.43 Lichen simplex chronicus occurs with increased frequency on genital skin. Erythema and lichenification of the scrotum are a result of chronic scratching and rubbing. Remove irritants and potential allergens.

Fig. 2.44 Lichen simplex chronicus—classical presentation. Skin lines are markedly accentuated. Itching becomes more intense as the plaque thickens and a vicious cycle continues.

Fig. 2.45 Lichen simplex chronicus of the vulva. Sharply demarcated erythema and increased skin markings are seen. This skin is markedly pruritic. An ointment-based topical steroid is most appropriate for treatment. If low potency not adequate, limited treatment with a moderate- to high-potency steroid should be monitored.

Fig. 2.46 Plaques of lichen simplex chronicus on the scrotum. Potent topical steroid ointment was used, but the plaque quickly reappeared after renewed habitual scratching. Stopping scratching is critical to resolution.

Fig. 2.47 Lichen simplex chronicus. Stress may induce chronic scratching in this area.

Fig. 2.48 Prurigo nodularis may be considered a localized, nodular form of lichen simplex chronicus. These lesions are intensely pruritic and are perpetuated by picking and scratching. Nodules are dome shaped, erythematous, and firm and may have a crusted surface.

Hand Eczema

Description

- Hand eczema is a common, often chronic problem with multiple causative and contributing factors.
- Hand eczema can be categorized as follows: irritant; keratolysis exfoliativa; atopic; fingertip; allergic; hyperkeratotic; nummular; pompholyx (dyshidrosis); lichen simplex chronicus; and id reaction. Each of these types of hand eczema is covered separately elsewhere in this book.
- Irritant hand eczema is most common, followed by atopic hand eczema.
- Allergic contact dermatitis accounts for 10% to 25% of hand eczema.

History

- Women are affected more often than men.
- Occupational risks include irritant chemical exposure, frequent wet work, chronic friction, and work with sensitizing (allergenic) chemicals.

Exogenous Factors

- Irritants include chemical irritants (e.g., solvents, detergents, alkalis, and acids), friction, cold air, and low humidity.
- Allergens include occupational and nonoccupational sources. Immediate type I hypersensitivity reaction can involve reactions to latex and food proteins, and the more common delayed-type (type IV) hypersensitivity reaction can involve reactions to rubber additives, nickel, medicaments (bacitracin, neomycin, and hydrocortisone) and commonly found chemical ingredients in personal care products or cleaning products (e.g., preservatives, fragrances, sunscreen, and other additives). Ingested allergens (e.g., nickel) may play a role.
- Infection can involve id reactions, including hand eczema as a reaction to a distant focus of fungal (i.e., dermatophytid) or bacterial (i.e., bacterid) infection.

Endogenous Factors

- Atopic diathesis (hay fever, asthma, atopic eczema) is often a predisposing factor and may contribute to susceptibility to the disease and chronicity of the problem, despite appropriate treatment and care measures.

Skin Findings

- The entire skin should be examined for clues and contributing factors and for exclusion of other dermatoses (i.e., psoriasis, cutaneous lymphoma, connective tissue processes).
- This condition is variable; acute, subacute, and chronic eczematous changes may be seen. Although there is no reliable association between clinical pattern and etiology, the following findings may prove useful:
  - Xerosis, erythema, burning more than itching on dorsal or volar hands: irritant factors should be suspected.
  - Nummular eczema, dorsal hands and fingers: allergy, irritation, or atopy can play a role—occasionally, contact urticaria (type I hypersensitivity reaction) is the culprit.
  - Recurrent crops of intensely pruritic vesicles on lateral fingers and palms: pompholyx, otherwise called dyshidrotic eczema, should be suspected. Consider patch testing.
  - Fingertip eczema (dryness, splitting, tenderness, no itch): an irritant, an endogenous factor (atopy during the winter), or frictional eczema should be suspected.
  - Erythema, scaling, itching, in the "apron" (base of the fingers) area of palm: atopy should be suspected.

Nonskin Findings

- Atopic patients may have a personal or family history of atopy, including eczema in childhood, hay fever, or asthma.

Course and Prognosis

- If exposures to irritants and allergens can be identified and avoided early in the course, the prognosis is often good for complete recovery.
- Continued or long-standing exposure to irritants and allergens can result in chronic dermatitis.

Fig. 2.49 Irritant hand eczema occurred in this woman who cleaned without glove protection. Scratching prolongs the disease.

Fig. 2.50 Irritant hand dermatitis. The vesicular nature of this eruption also suggests a contact allergic component. Patch testing would be helpful in this case to identify any contact allergens.

Fig. 2.51 Irritant hand dermatitis. The findings are mild erythema and xerosis. This is an early stage of irritant contact dermatitis. Repeated exposure to irritants, such as soaps, detergents, and water, are frequently the cause.

Fig. 2.52 Irritant hand dermatitis. Subacute eczematous inflammation with erythema, painful fissuring, and scaling.

Fig. 2.53 Hand eczema. Dry, thick, fissured hyperkeratotic eczematous plaques are difficult to treat. They last for months or years and may be impossible to distinguish from psoriasis.

Fig. 2.54 Hand eczema. Constant hand washing has perpetuated this chronic eczematous dermatitis on the back of the hands. The eruption cleared rapidly when a group IV topical steroid and plastic occlusion were applied at bedtime for 7 days.

Fig. 2.55 Eczematous dermatitis of the hand. This is usually very pruritic. Switching from multiple topical products should be discouraged. A bland nonfragranced thick emollient should be used as part of the treatment regimen, several times a day to try to heal the barrier.

- Avoidance and appropriate care often improve the condition, but some patients may not resolve it entirely.

Treatment

- Treatment involves the identification and avoidance of irritants, such as frequent hand washing and water exposure, soaps, detergents, and solvents. Chronic frictional trauma is also an irritant that can result in persistent dermatitis.
- Protective measures (e.g., vinyl gloves for wet or chemical work) can be taken.
- Topical corticosteroids with medium to high potency (groups II–IV) are administered twice daily. Ointments are preferred to creams. It is preferable to refrain from superpotent (group I) agents unless the dermatitis is severe. Topical steroids for hand dermatitis are most effective when used intermittently, rather than chronic management.
- For severe and weeping dermatitis, a superpotent topical corticosteroid is applied after tap-water or Burow's solution wet dressings twice a day for the initial 3 to 5 days of treatment, followed by the application of a medium-potency topical corticosteroid twice a day for several weeks.
- The following should be considered: topical tar hand soaks with Balnetar oil, two or three capfuls diluted in a basin of water for 15 to 30 minutes twice a day, followed by the application of topical corticosteroid.
- Systemic steroids (prednisone 0.5–1 mg/kg/day with tapering over a 3-week course) may occasionally be required to bring a severe acute inflammation under control.
- Most patients improve with avoidance of irritants, treatment with topical corticosteroids, and frequent lubrication.
- If allergy is suspected (hand edema, vesiculation, itching, and particularly dorsal hand eczema or recurrent eczema not responding to treatment), patch testing should be done to evaluate for contributing or causal allergens. Relevant occupational allergens should be included in the tested materials.
- The patient should be referred to a dermatologist in chronic unresponsive cases. Other treatments that may be considered include topical psoralen–ultraviolet A treatment and Grenz ray therapy. In disabling cases, management with weekly low-dose methotrexate (5–15 mg weekly) or oral low-dose daily cyclosporine (3–4 mg/kg) is reasonable.
- Dupilumab should be a consideration for severe, refractory, chronic cases that have otherwise been fully evaluated.
- Biopsy may be considered in severe cases.

Discussion

- Chronic, cyclic vesicular hand dermatitis (pompholyx) represents a most difficult management problem.
- Patch testing to occupational and environmental allergens should be considered if hand eczema does not improve or resolve with simple measures. A broad screening series including other potential allergen trays depending on history of exposure should be tested for the greatest yield. Occupation-specific trays (i.e., hairdressers, machinists) may be important.

Pearls

- Referral to a dermatologist for evaluation and patch testing is warranted when hand eczema does not resolve after a trial of sensitive skin care, including daily emollient use, protective use of gloves for frequent wet or chemical work, and a few weeks' course of topical steroid treatment.
- Psoriasis on the palms can mimic eczema. If there is sharp demarcation of plaques on the palms, with silvery or yellowish chronic scaling and symmetric involvement, a diagnosis of palmar psoriasis should be considered.
- Causal or contributing factors to hand eczema are not well identified unless the clinician seeks to know how and what the hands are exposed to: the occupation, household duties, hobbies, and hand care should be explored in detail. Although new routines or exposures can lead to a new case of hand eczema, chronic exposures may also lead to allergy. More than one relevant allergen is often identified in cases of chronic hand eczema.

Fig. 2.56 Chronic eczematous inflammation on the back of the hand in an atopic patient. Avoidance of irritants and allergens, along with a sensitive skin care daily regimen of moisturizing with a bland emollient, is recommended.

Fig. 2.57 Irritant hand dermatitis on the palmar surface of the fingers is difficult to treat and tends to be chronic. Intermittent topical steroids, constant moisturizing, and protection with gloves are the mainstays of treatment. Vinyl gloves are best as they avoid the most common glove allergens.

Fig. 2.58 Erythema, vesicles, and crusting of the fingertips to the "apron" area of the palm. This eczematous dermatitis may be irritant, allergic, or endogenous.

Fig. 2.59 Erythema, scaling, and sharp demarcation are features of this hand dermatitis. A potassium hydroxide examination is reasonable.

Fig. 2.60 Irritant contact dermatitis was caused by exposure to cleaning solutions. The rash persisted with scratching. The potassium hydroxide preparation was negative for fungi. Psoriasis may have a similar appearance, and even a biopsy may not be able to differentiate the two diseases.

Fig. 2.61 Contact allergy most commonly involves the dorsum of the hands but may involve the palms. Patch testing is essential for refractory or recurrent cases of chronic hand dermatitis. An allergen, after identified, must be avoided for resolution of the rash.

Table 2.1 Allergic Hand Dermatitis: Some Possible Causes

Allergens	Sources
Nickel	Door knobs, handles on kitchen utensils, scissors, knitting needles, industrial equipment, hairdressing equipment
Potassium dichromate	Cement, leather articles (gloves), industrial machines, oils
Rubber	Gloves, industrial equipment (hoses, belts, cables)
Fragrances	Cosmetics, soaps, lubricants, topical medications
Formaldehyde	Wash-and-wear fabrics, paper, cosmetics, embalming fluid
Lanolin	Topical lubricants and medications, cosmetics
Preservatives	Cosmetics, moisturizing creams and lotions, wet wipes, cooling fluids

Asteatotic Eczema

Description

- A distinctive clinical pattern of eczematous dermatitis that is caused by excessive dryness and chapping of the skin. This is also referred to as *eczema craquelé*.

History

- Asteatotic eczema is a form of subacute eczematous dermatitis that tends to be chronic and low grade with wintertime seasonal flares because of low humidity.
- Men and women are equally affected. It is more common in elderly people.
- It is more common in patients with the atopic diathesis (see later section, Atopic Dermatitis), especially in later life.
- Most patients have a history of previous similar flares.
- The prevalence peaks in late winter and improves in summer, especially in colder, drier climates.
- Any cutaneous site may be affected, although the lower legs are most commonly involved.
- Early on, affected individuals often note that their skin looks and feels dry.
- With progression, itch, with increasing inflammation, becomes the most prominent symptom.
- Burning and stinging occur in advanced cases with fissures and crusting.

Skin Findings

- The clinical picture is that of subacute eczematous dermatitis.
- Xerosis with accentuated skin markings is a constant feature from the onset.
- Inflammation is at first subtle but becomes more pronounced over time.
- Faint, poorly defined erythema progresses to fiery red, acute eczematous papules that coalesce into broad plaques.
- Vesicles are not typically seen, although excoriations are nearly universal.
- Dry, thin desquamation progresses toward the pattern of eczema craquelé, with thin superficial fissures reminiscent of the cracked finish on porcelain or of a dried riverbed.
- The skin is very dry, cracked, and fissured. The skin may be painful.
- With progression, the eczema develops acute features with weeping, crusting, and intense erythema.

Nonskin Findings

- Fever is unusual and suggests cellulitis.

Laboratory

- The clinical picture is distinctive enough that skin biopsy is rarely needed to establish the diagnosis.
- Skin biopsy confirms epidermal spongiosis with a superficial perivascular infiltrate and often with secondary impetiginization.

Course and Prognosis

- Seasonal recurrence during the winter months should be expected.
- Mild seasonal flares with itching and xerosis tend to improve with warmer weather, seasonal change, and repetitive skin lubrication with a bland moisturizer, cream, or ointment (preferred over lotion).
- Active subacute inflammation generally responds to topical medium-potency corticosteroid ointments and also improves with the season.
- A severe localized flare with acute features, such as weeping and crusting, also responds to individualized topical therapy, as outlined later.

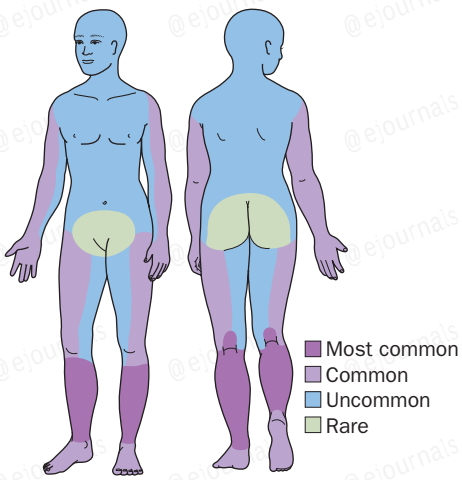

Fig. 2.62 Asteatotic eczema distribution diagram.

Fig. 2.63 Eczema craquelé is a form of eczema that occurs most typically in the winter when humidity is low. Elderly people are most prone. The skin appears cracked and inflamed.

Fig. 2.64 Asteatotic eczema. The skin is very dry, cracked, and fissured. This pattern evolved in an atopic patient who continued to wash excessively dry skin. The skin may be painful.

Discussion

- The differential diagnosis includes other subacute eczematous dermatoses, such as stasis dermatitis, irritant contact dermatitis, atopic dermatitis, allergic contact dermatitis, and less likely, cellulitis.
- More than one dermatosis may be present. The second dermatosis may mask or exacerbate the primary eczematous process.
- Irritant and allergic contact dermatitis may develop as a result of the patient's own efforts at self-treatment.
- Patients should be asked about what they have been applying to the involved areas.
- Stasis dermatitis occurs, commonly on the lower legs, in older patients. There is usually a history of vascular insufficiency and leg edema and the presence of hemosiderin staining of the skin.

Management

- Therapy is determined by the stage (acute, subacute, or chronic) of the asteatotic eczema and the degree of inflammation.
- For xerosis, therapy consists of sensitive skin measures, namely the limited use of mild soap and the liberal use of emollients.
- Petrolatum offers a preservative-free choice as a lubricant, although patient compliance may be difficult.
- Moisturizers containing lactic acid, urea, or glycolic acid may also be useful.
- Early inflammation is best treated topically with a medium-potency corticosteroid, preferably in an ointment base.
- Therapy should be continued until the erythema and scaling resolve.
- Liberal use of emollients should then be continued as a prophylaxis against recurrence. Bland, fragrance-free emollients are best (Vanicream, Aveeno, CeraVe, Cetaphil).
- Localized flares with acute eczematous features of weeping and crusting should be treated first as acute eczema.
- Patients require close follow-up during this stage because localized flares may become generalized.
- Referral to a dermatologist should be considered for the management of recurring acute flares and an evaluation for possible allergic contact dermatitis.
- Wet dressings with tap water or Burow's solution, along with a medium-potency topical corticosteroid in a cream base, are helpful for débridement and reducing inflammation.

- Oral antibiotics may be indicated for secondary impetiginization, indicated by honey-colored, sticky crusts.
- After the weeping, induration, and crusting improve, the wet dressings should be stopped to avoid excessive drying of the involved areas.
- A medium-potency topical corticosteroid ointment (group II or IV) should be continued until the redness and scaling resolve, about 2 to 3 weeks.
- Thereafter, sensitive skin care, including emollients, is helpful in limiting recurrence.
- Systemic steroid therapy is rarely indicated for asteatotic eczema.

Pearls

- Affected skin often appears like cracked porcelain early on. This stage often responds very nicely and promptly to routine use of emollients and removal of any irritating soaps or other irritants (i.e., winter swim programs in pools treated with bromine or chlorine).
- The patient should be asked what he or she is doing to treat the dermatitis and what skin care regimen is used.
- Home remedies might include household bleach, astringents, hot water, shake lotions, and other potential irritants that may be exacerbating the condition.
- Neomycin, corticosteroids, and preservatives and fragrances in various medicaments and topical products are potential sources of allergens.
- Referral to a dermatologist should be considered for patients with refractory dermatitis.

Fig. 2.65 Asteatotic eczema. This may be due to excessive washing of the skin or to winter conditions of cold, low-humidity air. The appearance is of cracking of the skin, superficial fissures, and erythema.

Fig. 2.66 Chronicity of asteatotic eczema leads to increased erythema, scaling, fissuring, and discomfort. Skin is typically pruritic. The fissures appear in a "crazing paving" pattern. Regular use of a bland emollient is extremely helpful in resolving this problem.

Fig. 2.67 Asteatotic eczema with severe long-standing inflammation. There are large, deep fissures and secondary infection.

Fig. 2.68 Asteatotic eczema. Serum oozes from the fissures and dries into linear and annular crusts. Subacute eczematous inflammation surrounds the fissures.

Chapped, Fissured Feet

Description

- Findings include scaling, erythema, and tender fissuring of the plantar feet.
- The tendency for severe chapping is age related; it is most common in prepubertal children but can occur in adults.

History

- Chapped, fissured feet are most common in early autumn and winter, when the weather becomes cold and heavy socks and impermeable shoes or boots are worn.
- Symptoms include soreness and pain.
- The mean age of onset is 7 years; the mean age of remission is 14 years.

Skin Findings

- The skin on the plantar feet—especially the weight-bearing skin of the toes and metatarsal regions—is dry, erythematous, scaly, and fissured. Fissuring may be deep and very tender.
- Chapping may extend to the sides of the toes.
- Eventually, the entire sole may be involved.

Discussion

- Atopy is suspected in these patients, but this is not well accepted.

Differential Diagnosis

- Tinea pedis infection—a potassium hydroxide examination should be done
- Allergic contact dermatitis
- Psoriasis

Treatment

- The feet should be kept dry; prolonged time in moist, occlusive shoes should be avoided.
- A thick emollient ointment (Flexitol Heel Balm, Aquaphor, petrolatum, Cetaphil or Aveeno cream) should be applied several times each day.
- If the condition is pruritic, topical steroids provide some relief. Group II or III topical steroid ointments are applied twice a day, preferably with plastic-wrap occlusion at bedtime, for 2 to 3 weeks.
- A 15-minute soak with tar bath oil (Balnetar—2 caps in a bucket of water) is followed by the application of a lubricating ointment or topical corticosteroid.
- Preventative measures include changing into light leather shoes after the removal of wet boots, alternating footwear to allow complete drying, and changing cotton socks frequently if moist.

Pearls

- Symmetric involvement of the soles. Inflammation may be confined to just part of the soles.
- Atopic dermatitis in children occurs mainly on the dorsal toes. Children with chapped, fissured feet complain of soreness and pain.
- Cracks and fissures appear in cases of long duration. Pain becomes more intense than itching.
- The key to improvement lies in frequent and continued heavy moisturization of the skin and prompt removal and change of moist footwear.

Fig. 2.69 Early stages of chapped, fissured feet. The feet are dry, smooth, and red.

Fig. 2.70 Confluent involvement of the feet with erythema, scaling, and fissuring. Multiple repeated wet–dry cycles in the winter can lead to these changes. Patients need to remove and avoid wet footwear.

Fig. 2.71 Chapped fissured feet. This is a painful condition, which is sometimes pruritic. Repeated use of bland emollients daily is necessary, along with avoidance of repeated wet–dry cycles of the feet to damp shoes and socks. A class I or II steroid ointment can be used to treat the inflammation for 2 to 3 weeks.

Fig. 2.72 Chapped, fissured feet. Cracks and fissures appear in cases of long duration. Pain becomes more intense than itching. The condition is more common in children.

Fig. 2.73 Chapped, fissured feet. Dry, pink, tight-looking skin on the plantar surface is prone to painful fissures. This is most common in the winter, triggered by wet–dry cycles and prolonged time in wet footwear in an atopic individual.

Fig. 2.74 Chapped, fissured feet. Tender skin, erythema, and xerosis are seen in chapped, fissured feet, which can be common in a person with an atopic predisposition.

Allergic Contact Dermatitis

Description

- Allergic contact dermatitis is a delayed-type hypersensitivity reaction caused by skin contact with a hapten (allergen) to which an individual has become sensitized. Allergic contact dermatitis results in eczematous dermatitis.
- Sensitization is required, and allergy is specific to a particular chemical; allergens typically have low molecular weights, are lipid soluble, and are reactive chemicals.
- Poison ivy, poison oak, and poison sumac dermatitis are prototypes of allergic contact dermatitis.
- Common causes of allergic contact dermatitis include metals, such as nickel, cobalt, and chromate; rubber additives in gloves and shoes (carbamates, thiurams, mercaptobenzathiazole); preservatives or other additives in products, such as skin lotions, wet wipes, creams, lotions, sunscreens, and other cosmetics and toiletries. Common allergens include the antimicrobial preservatives methylisothiazolinone, quaternium-15, imidazolidinyl urea, diazolidinyl urea; fragrances and fragrance additives; other product additives (i.e., foaming agents, surfactants; formaldehyde and related chemicals; nail polish additives); and topical medicaments (e.g., bacitracin, neomycin, hydrocortisone).

History

- Initial exposure and primary sensitization result in clinical inflammation generally 14 to 21 days after exposure. Exposure to a chemical is required for sensitization and clinical allergy to develop.
- The time required for a previously sensitized person to develop clinically apparent inflammation is about 12 to 48 hours but may vary from 8 hours to 120 hours—the rash is delayed somewhat from the contact. The rash can last as long as 3 weeks after one exposure and can be ongoing with minimal re-exposure.
- A new allergy to an allergen in a product (e.g., cosmetics, topical treatments, occupation-related allergens) or other exposures can occur even when there is a history of prolonged use without difficulty. The rash is recurrent if the exposure is recurrent; because many products have the same or chemically related ingredients, changing topical products often does not result in resolution of the eczematous rash. More than one contact allergy is common in some cases of chronic dermatitis.
- Some patients develop multiple contact allergies to chemically unrelated allergens (polysensitization).
- Careful history should include date of dermatitis onset, possible relationship to work (i.e., whether the condition improves during the weekend or prolonged vacations), type and specifics of contact to work exposures, hobby and home exposures, and type of skin care products used.
- Some allergy-causing substances are photoallergens; sunlight exposure together with the chemical exposure is required for the allergic reaction to occur. Photoallergy to sunscreen chemicals is most common.
- Individuals sensitized to topical medications or other allergens may develop generalized eczematous inflammation if those medications or chemically related substances are ingested (internal–external reaction). For example, a patient may be sensitized to topical diphenhydramine in a cream and then react with a generalized rash to oral diphenhydramine.

Skin Findings

- The intensity of the eczema depends on the individual's degree of sensitivity, concentration of the allergen, and quantity of antigen exposure.
- Allergic contact dermatitis is characterized by vesicles, edema, redness, and, often, extreme pruritus. A chronic exposure usually manifests as subacute or chronic eczema. Strong allergens, such as poison ivy or hair dye, often result in bullae.
- Dermatitis distribution is usually first confined to the area of direct exposure. If exposure is chronic, allergic dermatitis may spread beyond the areas of direct contact.
- Itch and swelling are key components of the history and can be a tip-off to allergy.

Fig. 2.75 Allergic contact dermatitis. Contact allergy to bacitracin or another topical antibiotic, such as neomycin, should be considered in the differential diagnosis of erythema and swelling with itch at a surgical site where topical antibiotic had been used. Such is often mistaken for infection. Itch rather than tenderness is a clue.

Fig. 2.76 Allergic contact dermatitis. Erythema is sharply demarcated on the tops of the feet. Contact allergy to a leather component or adhesive material are possible causes.

Burning is more often typical of irritant contact dermatitis but can be seen in allergic contact dermatitis.

- Dermatitis caused by plants is often distributed in linear streaks. The hands may spread allergens unintentionally.
- Allergy to a topical product used on the face may manifest as a pruritic patchy erythema, asymmetrically distributed. Involvement of the face rarely manifests with vesicles.
- Strong sensitizers, such as poison ivy, may produce intense inflammation despite low concentration or exposure; weak sensitizers may cause only pruritic or burning erythema.
- The hands, forearms, and face are the most common sites of allergic contact dermatitis. Allergic contact dermatitis may affect very limited skin sites, such as the eyelids, dorsal hands, and lips, tops of the feet, or genitalia. Contact allergy may be scattered and generalized.
- Airborne particulate matter (e.g., burning poison ivy) can lead to dermatitis of the face (including the eyelids and postauricular skin), the neck, and other exposed skin surfaces.
- Photoallergic contact dermatitis typically affects the exposed skin of the face, neck, forearms, and dorsal hands; there is usually submental, upper eyelid, and postauricular sparing.
- Most occupational allergic contact dermatitis affects the hands and forearms; the face and eyelids may be affected if there is an airborne allergen or indirect hand-to-face transfer of the allergen.

Laboratory

- Patch testing is performed by physicians trained in the technique and is indicated for people with persistent or recurrent dermatitis despite appropriate topical therapy.
- Patch testing should be performed to a broad panel of screening allergens, allergens of occupational or a vocational relevance, and the patient's personal care products. Some important allergens may be missed by patch testing with a small panel of allergens

Fig. 2.77 Acute, intense erythema, weeping, and crusting in this case of allergic contact dermatitis. Allergy to preservatives, and most recently to the preservative methylisothiazolinone are typical suspect causes. Methylisiothiazolinone allergy can be missed with the T.R.U.E. test.

Fig. 2.79 Allergic contact dermatitis of the axilla. The most common reason for this is a fragrance in a deodorant. Other excipients in deodorants may lead to a similar picture.

Fig. 2.78 Erythema in the distribution of bra elastic. Rubber allergy from underwear is not common. Initially, contact allergy tends to be localized to the site of contact. With chronicity, the process can spread beyond the area of contact.

or by not testing occupationally relevant allergens.
- The availability of broad allergen trays and larger screening series is presently limited in the United States. This is a serious barrier to proper diagnosis and treatment.
- Proper patch testing technique requires three visits: one to apply allergen chemicals in proper concentration; another to remove the tests and to read and grade the results; and the last for a final, delayed reading. Omitting the delayed reading will result in missed identification of allergens.
- Photopatch testing to determine abnormal sensitivity to light should also be performed in patients with photo-distributed dermatitis.

Differential Diagnosis

- Irritant contact dermatitis (patch testing is not performed for irritant-type dermatitis; the clinical findings can be indistinguishable clinically, especially on affected hands)
- Atopic dermatitis (distribution can be helpful; atopic patients can and do develop contact allergies)
- Cellulitis (swelling and erythema can be similar, but cellulitis usually is painful, without itch)
- Connective tissue disease (persistent eyelid erythema; clues are no itch of affected skin and possible cuticle hypertrophy in dermatomyositis)
- Rosacea (distribution of erythema, flushing, and burning are helpful)
- Cutaneous T-cell lymphoma (biopsy, molecular testing, distribution of rash can be helpful)

Treatment

- Avoidance of the allergenic substances is essential to recovery.
- Identification of the allergens is essential. If the cause is not obvious—which typically it is not—treatment should be started, and further evaluation and patch testing should be planned. Physicians and patients are poor predictors of a patient's specific allergies. The only way to confirm and identify contact allergy is by patch testing.
- Begin topical treatment by simplifying what is applied to the skin and using a topical corticosteroid. Discontinue all moisturizers, lotions, and topical medications, except plain petrolatum, if needed, for dryness. To treat the dermatitis, advise a topical corticosteroid ointment twice a day for 2 to 3 weeks.
- Choice of corticosteroid potency is based on the body site affected: low potency for the face; medium potency for the arms, legs, and trunk; and high potency for the hands and feet.
- When possible, corticosteroid ointment, rather than cream, should be prescribed because additives in creams may be allergenic.

Fig. 2.80 Contact allergy to nickel is very common. Ear piercing is the greatest risk factor. An increasing number of piercings is associated with an increased risk for nickel allergy. This photo shows contact allergy to nickel released from a pants fastener.

Fig. 2.81 Contact dermatitis of the forearm and dorsal hands. The dermatitis can be acute, as in this case, or subacute or chronic.

Fig. 2.82 Intense erythema, edema, and pruritus are the result of contact allergy to eye drops. History of all facial contactants and patch testing to a standard series, as well as to the patient's personal products, is essential to identify the allergen.

Fig. 2.83 Contact dermatitis of the eyelids. Differential diagnosis includes allergic, irritant, and atopic dermatitis. Allergic contact eyelid dermatitis can be from direct intentional use of products on the eyelids, airborne contact, products used on the face and hair that are washed off over the eyelids, or incidental unintentional contact of an allergen brought to the eyelids by the hands.

- The patient's skin regimen should be simplified to avoid further possible allergen exposure. No other topical products (except plain petrolatum or the prescribed corticosteroid) should be used during treatment. Hydrocortisone is best avoided because cases of contact allergy can occur, and other alternatives (desonide, mometasone, and tacrolimus) are available. Allergy to other topical steroids or ingredients, such as triamcinolone acetonide, is also possible and should be considered if the rash fails to improve or gets worse with treatment.
- For severe or generalized allergic contact dermatitis, a 3-week tapering course of oral corticosteroids is appropriate. This should not be relied on repeatedly.

Fig. 2.84 Eyelid dermatitis. There is subtle erythema and scaling. Eyelid dermatitis is a frequent problem in individuals with an atopic diathesis.

- Some allergens (e.g., hair dyes and glues) can penetrate rubber gloves, so glove protection may not be adequate.
- Some allergens, such as nickel and chromate, are associated with chronic dermatitis, despite avoidance.
- Time should be spent on patient education, detailing potential sources of exposure.
- After an allergen is determined by diagnostic patch testing, reviewing allergen exposure lists in depth, educating patients about avoidance of the allergen and potentially related substances, and providing suitable alternatives are vital to a good outcome.

Pearls

- Allergy can develop after years of exposure to products and medications; new and chronic exposures also can cause allergic contact dermatitis.
- Consider patch testing in a patient with recurrent hand and facial dermatitis.
- Always ask about occupation and exposures; there may be both irritant and allergic factors of importance. Some occupations with a higher risk for allergic contact dermatitis include hairdressing and dentistry, and people employed as health care workers, cleaners, nail technicians, manufacturing laborers, printers, florists, and machinists are also at higher risk.
- Other factors may contribute to an eczematous dermatitis (atopic dermatitis, stasis dermatitis), and contact allergy may aggravate these conditions substantially. Consider patch testing in a patient with a history of dermatitis whose eczematous problem is flaring or poorly controlled.

Fig. 2.85 Erythema, mild swelling, and vesicles are seen in this case of allergic contact dermatitis of the lips. Lanolin, flavoring and fragrance materials, and sunscreen chemicals are potential causes.

Fig. 2.88 This is a subacute form of allergic contact dermatitis on the neck and upper chest. The face was also affected. Common ingredients, particularly certain fragrance materials and preservatives, moisturizers, and other skin care products, can contain allergens that result in this type of patchy eczematous dermatitis.

Fig. 2.86 Allergic contact dermatitis. Patch tests are placed on the back and left on for 2 days. A reading at the time of removal and a late reading at day 4 or 7 are advised to miss late reactions.

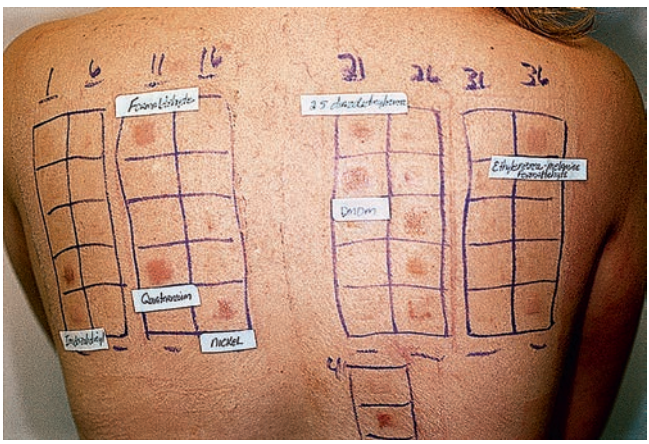

Fig. 2.87 Patch testing. One allergen was placed in each marked box. A limited standard series may not be enough. Experts choose allergens for testing based on patient history and suspect exposures. A large number of allergens, including the patient's own products is usually necessary to properly investigate a suspected allergic contact dermatitis.

Irritant Contact Dermatitis

Description

- Irritant contact dermatitis is an eczematous dermatitis often caused by repeated exposure to mild irritants, such as water, soaps, heat, and friction. Strong irritants include acids, alkalis, and wet cement; these chemicals can result in the acute lesions of chemical burns. Chronic exposure to mild irritants is the more common problem resulting in eczematous changes.
- The intensity of the inflammation is usually related to the concentration of irritant and the exposure time. Mild irritants cause dryness, fissuring, and erythema; strong irritant chemicals may produce an immediate reaction characterized by burning, erythema, edema, and possibly ulceration of the skin.
- About 80% of cases of contact dermatitis involve irritant contact dermatitis.
- In contrast to allergic contact dermatitis, irritant contact dermatitis is nonspecific and does not require sensitization.

History

- A background of atopy (hay fever, asthma, or eczema) predisposes to an increased susceptibility to skin irritation. Susceptibility to an irritant is individual and can be variable.
- Irritant contact dermatitis is the most common type of occupational skin disease, accounting for 80% of cases.
- Employment and household duties, including child care and hobbies, are critical parts of the history. Jobs characterized by repeated wet work, such as food service, health care, machinists, child care, and hairstyling, predispose the patient to irritant contact dermatitis.
- Common irritants include detergents, acids, alkaline chemicals, oils, organic solvents, oxidants, reducing agents, and frequent water or wet work.
- Coarse fibers, such as particulate fiberglass or sawdust, can cause irritant contact dermatitis.
- Exposure may occur from direct contact or the by airborne route.
- Examples of irritants that can cause an airborne irritant contact dermatitis include fiberglass, formaldehyde, epoxy resins, industrial solvents, glutaraldehyde, and sawdust.
- Repeated friction and mechanical irritation can result in chronic irritant contact dermatitis.
- Irritant eczematous dermatitis may occur with continuous exposure to mild irritants. After the irritation threshold is reached, persistent dermatitis may result from less exposure to mild irritants.
- Low environmental humidity reduces the threshold for irritation.
- Continuous exposure to moisture and wet–dry cycles in areas, such as the hands, the diaper area, or the skin, around a colostomy may eventually cause eczematous inflammation.
- An irritant dermatitis may become complicated by allergy as the number of applied topical remedies increases and damaged skin allows better penetration of allergens.
- Atopic individuals are predisposed to irritant contact dermatitis and often have prolonged dermatitis that is more difficult to manage.

Skin Findings

- The hands are most often affected. Both dorsal and palmar surfaces can be affected. The eyelids are another irritant-prone site. Chronic lip lickers will develop an irritant dermatitis from repeated wet–dry cycles.
- Erythema, dryness, painful cracking or fissuring, and scaling are typical. Vesicles may be present, but typically are not.
- Symptoms of tenderness and burning are common. Often, burning predominates over itch.
- Acute irritant dermatitis may show juicy papules or vesicles on an erythematous patchy background, with weeping and edema.
- Persistent, chronic irritant dermatitis is characterized by lichenification, patches of erythema, fissures, excoriations, and scaling.
- A hyperkeratotic form characterized by repeated scaling, cracking, and low-grade

erythema may result from repeated mechanical trauma, such as paper handling.
- Open skin may burn on contact with topical products that are otherwise usually tolerated.

Laboratory

- A potassium hydroxide examination may be performed to exclude tinea infection.
- Patch testing should be performed to evaluate the role of allergic contact dermatitis if the history suggests it (i.e., exposure to allergens) or if the condition is refractory or persistent despite treatment and preventive measures. Patch testing is usually performed with a ready-to-use screening series of allergen patches (e.g., the Thin-Layer Rapid Use Epicutaneous Test (T.R.U.E. Test); http://www.truetest.com). Testing to an expanded series can pick up relevant allergens and should be considered initially or if T.R.U.E. testing is negative and the rash persists.
- Skin biopsy, which is rarely performed, shows spongiosis, dermal edema, and an inflammatory infiltrate of predominantly lymphocytes.

Differential Diagnosis

- Allergic contact dermatitis (vesicles and itch are often more common in allergic contact dermatitis than in irritant contact dermatitis)
- Atopic dermatitis
- Tinea infection

Fig. 2.89 Irritant contact dermatitis. Chronic soap and water exposure and repeated hand washing led to this subacute eczematous dermatitis on the backs of the hands.

Fig. 2.90 Erythema, papules, and xerosis on the dorsum of the hands are often the start of an irritant type of eczematous dermatitis.

Fig. 2.91 Severe irritant contact dermatitis is characterized by large bullae. This was caused by a lye-containing soap.

Fig. 2.92 Ill-defined patchy erythema, papules, and erosions on the bilateral forearms. This eczematous dermatitis may be atopic, irritant, or contact in etiology, or a hybrid of these.

Treatment

- Early diagnosis, treatment, and preventive measures can prevent the development of a chronic irritant dermatitis.
- The avoidance of or decreased exposure to cutaneous irritants is critical for recovery of an effective skin barrier.
- The number of wet–dry cycles resulting from activities, such as repeated hand washing, should be decreased.
- Cotton gloves under vinyl gloves may allow for a decreased frequency of hand washing for wet work (gloves can be ordered online at http://www.allerderm.com).
- The mildest cleanser possible (Cetaphil, Dove, CeraVe, Vanicream Bar) should be used, and when appropriate, no cleanser should be used.
- Appropriate protective gloves should be worn for specific solvent or chemical exposure.
- When the patient's occupation is deemed relevant, material safety data sheets are consulted for exposure and protection information.
- Frequent application of a bland emollient (Vaseline, Cetaphil, Vanicream, or CeraVe) to affected skin is essential.
- For irritant hand dermatitis, a medium-potency or high-potency topical steroid ointment applied twice a day for several weeks can help reduce erythema, itching, swelling, and tenderness.
- For health care workers, hands that are visibly dirty or contaminated should be washed with antimicrobial soap; if not visibly soiled, an alcohol-based hand rub should be used in most situations requiring hand hygiene and disinfection. Repeated washing with soap and water is more irritating than use of alcohol-based rubs.

Fig. 2.93 Irritant contact dermatitis. Lip licking causes dryness and chapping. Eczema will develop if licking is continued.

Fig. 2.94 Irritant contact dermatitis. Lip licking for several weeks resulted in severe chapping with painful fissures. Continued lip balm use may encourage dependency and continued need for emollient. Discourage ongoing product use on the lips to moisturize. Plain petrolatum (Vaseline) is most appropriate.

Pearls

- Vesicles are not a typical finding in irritant contact dermatitis, unless there has been exposure to strong irritants. Subacute eczema and chronic eczema are the most characteristic clinical findings of irritant contact dermatitis.
- Stopping the cycle of repeated exposure to low-level irritants (e.g., water, soaps and detergents, repeated frictional contact) is essential to recovery. Repairing the skin barrier takes time and effort—irritants need to be avoided, and a bland emollient needs to be applied frequently.
- Irritant and allergic contact dermatitis can be impossible to distinguish clinically; if the condition remains chronic or persistent despite appropriate care and protective measures, patch testing is indicated to evaluate the contributing role of delayed-type (type IV) hypersensitivity reaction.

Fingertip Eczema

Description

- This common form of eczema is limited to the fingertips.
- One finger or several fingers can be affected.
- Itch is limited or is often absent.
- Tenderness, pain, and burning are common. Patients often seek attention because of pain.

History

- Usually, fingertip eczema is a recurring winter problem, but it may occur all year round.
- It is uncommon in children and occurs most frequently in adults.

Etiology

- Atopy may be a predisposing factor.
- Irritant chemicals or frictional contact may play a role. Repeated frictional contact with paper handling has been implicated as an aggravating factor.
- A less frequent etiology is allergic contact dermatitis to plants, resins, and acrylate-based glues.
- Occupational and hobby-related allergens, heat, repeated water exposure, repeated wet–dry cycles, and friction should be considered.

Skin Findings

- Dry, scaling, pink, and fissured fingertips characterize fingertip eczema.
- Peeling reveals red tender skin.
- The tips are very dry, smooth, red, and fragile. The inflammation tends to be chronic.
- Vesiculation is not typically seen.
- The process stops before the distal interphalangeal joint is reached.

Course and Prognosis

- The condition may last for months or years and can be very resistant to treatment.
- Precipitating factors are often not easily or consistently avoided.
- Inflammation may start on the fingertips but may slowly spread to involve the fingers and palms.

Discussion and Differential Diagnosis

- Contact allergy and psoriasis should be ruled out. Look carefully for other signs and sites of psoriasis to exclude this diagnosis.
- An uncommon presentation of contact allergy should be considered in handlers of tulip bulbs, florists, dentists, nail technicians, those who handle printing inks, or others who work with acrylate-type adhesives, plastics, and chemicals.
- An allergy to artificial nails should also be considered. Patch testing is indicated in suspect cases.
- If the nail is separated from the nail bed (onycholysis), candidal infection should be considered.

Management

- Management involves the avoidance of repeated wet–dry cycles, irritating detergents or solvents, heat, and friction.
- The condition should be managed as a subacute or chronic eczema; irritants should be avoided, and affected areas must be lubricated frequently.
- A bland and heavy emollient, such as Vaseline petrolatum or Aquaphor, should be applied frequently.
- Medium-potency topical steroids, with or without occlusion, give temporary relief.
- Cotton gloves and heavy moisturizers at night can help control this highly resistant form of eczema.
- Tar creams, such as MG217, applied twice each day may be tried if other measures fail.

Pearls

- Cyanoacrylate glue (e.g., Krazy Glue) is often used to seal the fissured painful fingertip cracks; contact allergy to this chemical is uncommon but is possible.
- Protection of the hands and affected skin by repeated application of petrolatum and use of cotton gloves can be very helpful.
- Decreasing irritation from repeated hand washing and decreasing exposure to other irritants are cornerstones of treatment. Household gloves should be used for wet work and cleaning duties.

- Patch testing with an expanded allergen series in which occupational exposures to glues, adhesives, resins, artificial nail chemicals, or plants (including florists, dental hygienists, and dentists) may be relevant, despite a lack of history of contact with "new" exposures. Patch test experts must be consulted for expanded testing.

Fig. 2.95 Fingertip eczema. Patients protect these deep, painful cracks with bandage strips. They wear cotton gloves and heavy moisturizers to bed in an attempt to control this highly resistant form of eczema.

Fig. 2.96 Fingertip eczema is very painful because of the skin fissures. It responds poorly to treatment with topical steroids.

Fig. 2.97 Fingertip eczema. The main feature is pain, not itch. Allergens are not typically involved in this type of presentation of erythema, dryness, and fissuring with pain, but not itch. Patch tests are typically negative.

Fig. 2.98 The tips of some or many of the fingers are dry, wrinkled, and often tender. This is usually, at least initially, a winter problem. Avoidance of friction and the use of repeated bland emollients are cornerstones of treatment.

Fig. 2.99 Scaling fingertips. The complaint is usually tenderness, not itch. Contact allergy is not usually an etiology. Sometimes repeated friction, such as paper handling, is contributory. The feet should also be examined.

Keratolysis Exfoliativa

Description

- Keratolysis exfoliativa is a common, chronic, asymptomatic, noninflammatory, symmetric peeling of the palms and soles. The cause is unknown.

History

- Keratolysis exfoliativa occurs most commonly during the summer.
- It is often associated with sweaty palms and soles.
- Some people have repeated episodes, and others experience this phenomenon only once.

Skin Findings

- Scaling starts simultaneously from several points on the palms or soles with 2 to 3 mm of round scale that appears to have originated from a ruptured vesicle; however, vesicles are not seen.
- The scales continue to peel and extend peripherally, forming larger, roughly circular areas that resemble ringworm, and the central area becomes slightly red and—in a few cases—tender.
- Scaling borders may coalesce.

Course

- This condition resolves in 1 to 3 weeks but may recur.

Treatment

- No therapy other than lubrication is required.

Pearls

- This condition improves with moisturization and generally resolves with age.
- It is worthwhile to do a potassium hydroxide examination to exclude tinea infection.

Fig. 2.100 Spontaneous peeling of the palms is common and unexplained. It may be seasonal and asymptomatic. Moisturizers are usually sufficient, and the process resolves with age.

Fig. 2.101 Spontaneous peeling of the palms. Long-standing cases may not respond to treatment and may be misdiagnosed as tinea.

Fig. 2.102 Spontaneous peeling of the palms. Some cases persist, and the skin becomes red and fragile.

Fig. 2.103 The differential diagnosis includes keratolysis exfoliativa, but a potassium hydroxide examination should be done to rule out a tinea infection causing this type of superficial scaling of the palms.

Nummular Eczema

Description

- Nummular eczema is a form of eczema characterized by often generalized, exceedingly pruritic, round (coin-shaped) lesions of eczematous inflammation. It is often chronic and difficult to treat.

History

- Adults are most often affected. Men are more commonly affected than women.
- The onset is usually gradual, with no clear precipitant, and usually no history of eczema.
- Nummular eczema often begins with a few isolated lesions on the legs; with time, multiple lesions occur, seemingly without any particular distribution.
- Lesions often resolve or improve after the administration of topical corticosteroids, only to recur in the same area after corticosteroid withdrawal.

Skin Findings

- Sharply demarcated, scaling, round eczematous plaques appear on the trunk and extremities.
- Weeping of lesions and vesiculation can characterize flares.
- Secondary infection with *S. aureus* may result in disease flares.
- A yellow honey-colored crust indicates secondary impetiginization.

Laboratory

- Patch testing reveals a relevant positive result in one fourth to one third of cases.
- A culture of the lesion may reveal *S. aureus.* Antibacterial treatment usually helps, but does not often resolve the problem.

Differential Diagnosis

- Psoriasis (often more obviously symmetric and geographic with silvery scales)
- Tinea infection (central healing and peripheral scaling; potassium hydroxide examination is helpful for differentiation)
- Cutaneous T-cell lymphoma (may be confused with nummular eczema; a skin biopsy or multiple skin biopsies over time may be necessary)

Course and Prognosis

- This is one of the most difficult forms of eczema to treat.
- The course is variable and unpredictable; this condition may be chronic, relapsing for years.
- After lesions are established, they tend to remain the same size and recur on previously affected skin.

Treatment

- See the earlier sections, Subacute Eczematous Inflammation (Subacute Eczema) and Chronic Eczematous Inflammation.
- Patch testing should be considered in refractory cases.
- Discontinue any unnecessary routine topical moisturizing products, over-the-counter oral medications, or dietary supplements and herbal preparations for at least 3 to 4 months.
- Active tinea pedis should be sought; tinea is treated with antifungal agents if it is present because, occasionally, generalized nummular eczema may be an id reaction to a distant site of tinea infection.
- The use of topical steroids with medium to high potency and bland nonfragranced emollients (CeraVe, Vanicream, Aveeno, or Vaseline) should be aggressive.

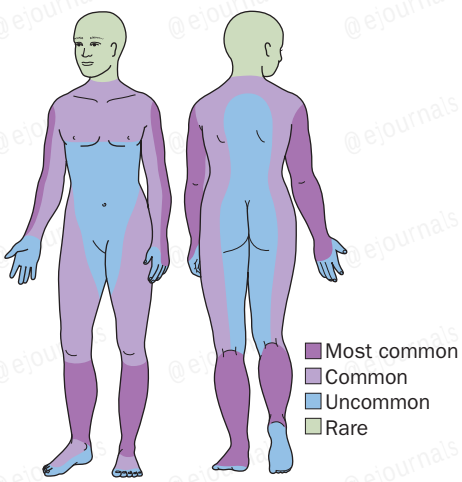

Fig. 2.104 Nummular eczema distribution diagram.

- A topical steroid is applied to affected skin twice a day for 3 to 4 weeks. It is best to treat a week or so longer than deemed necessary to resolve the lesions.
- The efficacy of topical steroid is increased by using occlusion with plastic wrap or a sauna suit (available at Walmart as a vinyl exercise suit) and by hydrating the skin with a bath before medication application, or by using both techniques.
- A secondary infection is treated with systemic antistaphylococcal antibiotics (e.g., dicloxacillin 250 mg four times a day; cephalexin 250 mg four times a day).
- Antihistamines can be prescribed for itching. Caution is used in elderly people.
- Systemic corticosteroids should be avoided for long-term management.
- Refractory cases should be referred to a dermatologist.
- Light therapy can help resolve lesions when topical treatments have failed. Narrow-band ultraviolet B and broad-band ultraviolet B are the best choices for light therapy.

Discussion

- The cause is unknown. Changes in soap or detergent usually make no difference.
- Lesions last for months and years and, unlike other forms of eczema, are treatment resistant.

Fig. 2.105 A round, scaling, erythematous patch of nummular eczema. Usually nummular eczema is widespread, and often the coin-shaped lesions recur on the same areas of skin during repeated flares.

Pearls

- Topical allergens, such as fragrance and medicaments (e.g., bacitracin, neomycin, and hydrocortisone), may drive some cases of nummular dermatitis. Affected patients should be counseled against using them at all.
- Lesions may be acute with exudate and crusts or chronic with erythema and scale. Itching is of variable intensity but typically is quite aggravating.
- Sunlight or ultraviolet B therapy can be very helpful in what is usually a treatment-refractory condition.

Fig. 2.106 This is a typical appearance of nummular dermatitis. Lesions are variably sized, erythematous, scaling round patches scattered on the trunk and arms. This often is a treatment refractory condition, and the cause is unknown and unlikely to represent contact allergy.

Fig. 2.107 Nummular eczema. Coin-shaped, erythematous scaling, and a discreet patch are seen on the upper back.

Fig. 2.108 Nummular eczema. The lesions often have varying stages, including an acute vesicular, weeping stage.

Fig. 2.109 Nummular eczema may look like ringworm or psoriasis. The borders of ringworm and psoriasis are usually sharply defined. The lesions' borders are indistinct in this case of nummular eczema.

Fig. 2.110 Nummular eczema. The weeping, round patch is typical of nummular eczema.

Fig. 2.111 Nummular eczema. Lesions may be acute with exudate and crusts, or chronic with erythema and scale. Itching is of variable intensity. Cutaneous T cell lymphoma may mimic nummular eczema so a biopsy is appropriate if the condition does not resolve in a few months.

Pompholyx

Description

- Pompholyx is also referred to as *dyshidrosis, dyshidrotic eczema,* or *vesicular endogenous eczema.*
- As much as 20% to 25% of hand eczema may be characterized as pompholyx.
- It is a distinctive, chronic relapsing, vesicular eczematous dermatitis of unknown etiology.
- Pompholyx is characterized by sudden eruptions of usually highly pruritic, symmetric vesicles on the palms, lateral fingers, or plantar feet. Hands-alone involvement occurs in 80%.

History

- Affected patients frequently have an atopic background (personal or family history of asthma, hay fever, or atopic eczema). It is more common in women than in men.
- Moderate or severe itching typically precedes a flare or recurrent eruption.
- Hyperhidrosis (increased sweating) often aggravates or accompanies this condition.
- Peak incidence is in the early 20s for women and mid-40s for men.
- Drugs eliciting pompholyx are rare but reported (immunoglobulin therapy).

Skin Findings

- Vesicles are 1 to 5 mm in diameter, monomorphic, deep seated, and filled with clear fluid, and they resemble tapioca. Vesicles erupt suddenly and symmetrically on the palms or lateral fingers or on the plantar feet.
- Rings of scale and peeling follow the eruption as itch diminishes. No surrounding erythema is typical.
- Depending on the phase of the disease, the clinician may see only brown spots. When the acute process ends, the skin peels, revealing a red cracked base with brown spots. The brown spots are sites of previous vesiculation.
- Nails may become dystrophic with horizontal ridging with chronic paronychia.

Course and Prognosis

- Vesicles resolve slowly over 1 to 3 weeks. Recurrences may be a few times a month or a few times a year.
- Chronic eczematous changes with erythema, scaling, and lichenification may follow.
- Waves of symmetrically distributed vesiculation can recur indefinitely.
- For unknown reasons, the chronic recurring eruption sometimes ceases with time.

Differential Diagnosis

- Pustular psoriasis of the palms and soles (pain more than itch is often the chief complaint)
- Id reaction (resulting from a distant focus of tinea infection)
- Inflammatory tinea (potassium hydroxide examination is positive)
- Acute allergic contact dermatitis
- Bullous pemphigoid (may be hemorrhagic)
- Cutaneous T-cell lymphoma (rarely bullous on the hands)

Management

- The initial treatment consists of cold wet dressings twice a day with either tap water or Burow's solution, followed by the application of a medium-potencyor high-potency steroid cream (groups I–III).
- Prednisone 0.5–1 mg/kg/day tapered over 1 to 2 weeks can be infrequently prescribed.
- Tacrolimus ointment (Protopic 0.1%) rotating with a topical medium-strength corticosteroid (groups II–III) twice daily for cycles of 3 to 4 weeks can provide some relief.
- Corticosteroids should not be relied on for repeated or chronic treatment.
- Oral antihistamines can alleviate pruritus.
- Topical hand psoralen plus ultraviolet A is a treatment option for frequent, refractory eruptions.
- In individuals allergic to nickel, attempts to control pompholyx with elimination diets (e.g., a nickel-reduced diet) may be worth a trial in difficult cases.
- If distant focus of tinea is identified with a positive potassium hydroxide test, treat that focus with aggressive topical antifungal medication (econazole or terbinafine cream every day for 3 weeks) or with a short course of oral antifungal medication (terbinafine or itraconazole) of appropriate duration and dose for the site of infection.

Fig. 2.112 Pompholyx. The acute process involves initial vesiculation, which is usually marked on the palms and lateral aspects of the fingers. The process ends with peeling, sometimes leaving a cracked, red base.

- Moderating or eliminating stress can be helpful and is anecdotally curative for some people.
- For chronic or severe disabling dyshidrotic eczema, a dermatologist should be consulted.
- Biopsy should be considered in cases that are chronic.
- If avoidance of allergens implicated by patch testing does not result in improvement and the condition remains disabling, further therapies include systemic immunosuppressants: low-dose weekly methotrexate (5–15 mg/week), mycophenolate mofetil (1000 mg twice daily), low-dose cyclosporine (3–4 mg/kg/day), azathioprine (100–150 mg/day to gain control, then maintenance of 50–100 mg/day), and intradermal botulinum toxin (100–160 international units). Use of any of these systemic drugs requires appropriate blood monitoring.

Discussion

- The causes of this recurrent, sometimes disabling, dermatitis are unknown; provoking factors seem heterogeneous. Because eliciting factors are numerous, this cutaneous sign is nonspecific, and the sources identified earlier need exploration in each individual. The role of atopy, occupational or other contact chemicals, and distant tinea infection should be considered. Consider biopsy.
- Systemic contact allergens may play a role because some individuals with positive patch tests show vesicular reactions on the hands when challenged orally with nickel, cobalt, or chromium.
- Contact allergy is as common in dyshidrotic eczema as in other forms of hand eczema. Allergens positive on patch testing most commonly include nickel, chromate, colophony, fragrance, balsam of Peru, rubber-related mercaptobenzathiazole and thiuram mix, and paraphenylenediamine.
- Some relationships with stress and smoking have been postulated, but these have been poorly studied.

Pearls

- The term *dyshidrosis* is a misnomer—the sweat glands are uninvolved and are not dysfunctional. However, most affected patients do have hyperhidrosis, which seems to aggravate the condition, and complain of aggravation from protective glove occlusion and sweating.
- Occupations associated with contact allergy as a possible cause or aggravating factor for dyshidrotic eczema include those in the construction industry, the service industry (including food and money handling, e.g., cashiers), health-related occupations, hairdressing, metallurgy, and chemical and textile industries.
- Search for distant sources of tinea, especially on the feet when the hands are involved. Treat the tinea infection, if found, with either a short course of oral antifungal medication or with aggressive topical antifungal medication.
- This condition can be very frustrating given the chronic relapsing nature. Establishing a good therapeutic relationship is vital, and then assessing the risks and benefits of more aggressive treatment strategies is crucial.

Prurigo Nodularis

Description

- Prurigo may be considered an idiopathic, papular, or nodular form of lichen simplex chronicus.
- In prurigo nodularis, there are very pruritic, firm papules and nodules on easily accessed skin. Lesions are secondary to repeated, localized scratching and picking.

History

- The onset is usually gradual and occurs in the setting of pruritus.
- Prurigo nodularis occurs primarily in adults.
- Stress is often anecdotally implicated. Psychogenic factors often play a role.
- Individuals with atopy and diabetes may be predisposed.
- Affected patients may be compulsive pickers.

Skin Findings

- A few to numerous dull, erythematous, or hyperpigmented nodules are randomly distributed. Extensor arms and legs are typically affected; the lumbosacral area, nape of the neck, and dorsal hands are reachable areas that are typically involved.
- Lesions are created by repeated rubbing, picking, and scratching.
- The small papules and nodules are red or brown, hard, and often dome-shaped with a smooth, crusted, or warty surface.
- Often, there are clues to a chronic process—hypopigmented scars or postinflammatory hyperpigmentation on skin accessible to repeated scratching and picking.

Laboratory

- Skin biopsy is rarely necessary but may help and should be considered. Histology shows chronic inflammation and marked epidermal hyperplasia.
- In generalized prurigo of recent onset, systemic causes of pruritus should be evaluated and excluded. Consider complete blood count with differential; thyroid function tests; liver function tests, including lactate dehydrogenase and alkaline phosphatase; renal evaluation; total serum immunoglobulin E; hepatitis B and C panels; HIV testing; serum protein electrophoresis (SPEP), chest radiograph; and possibly computed tomography if lymphoma is suspected.

Differential Diagnosis

- Causes of generalized pruritus should be excluded in recent, severe, and generalized cases; these include insect bites, psychiatric disorders, chronic renal disease, gluten-sensitive enteropathy, drug reactions, hypothyroidism or hyperthyroidism, occult liver disease (including hepatitis C, chronic obstructive biliary disease), HIV infection, polycythemia rubra vera, iron deficiency, occult malignancy (including solid-organ metastatic disease and leukemia or lymphoma, in particular, Hodgkin's lymphoma), and lichenoid drug eruptions
- Uncommon mimics of prurigo lesions have been reported and include dermatitis herpetiformis, nodular scabies, metastatic cancerous lesions, Langerhans' cell histiocytosis, and atypical lymphoproliferative diseases

Course and Prognosis

- Prurigo nodularis is often resistant to treatment and lasts for years.
- Cessation of itching, digging, and scratching is critical to lesion resolution and successful treatment.

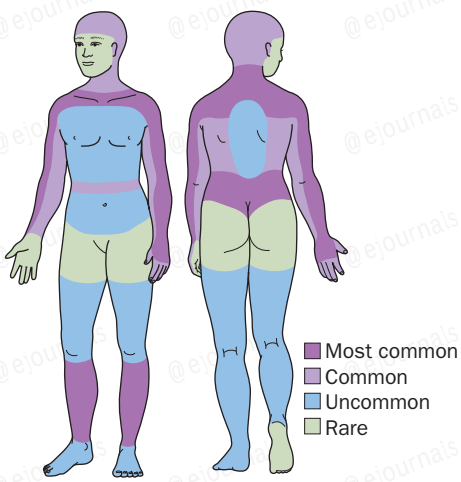

Fig. 2.113 Prurigo nodularis distribution diagram.

Fig. 2.114 Prurigo nodularis. Thick, hard nodules are typically found on the extensor surfaces of the arms and legs. Chronic picking causes them.

Fig. 2.116 Prurigo nodularis. Scattered violaceous firm papules are seen, with some scaling.

Fig. 2.115 Prurigo nodularis. Lesions measure 0.5 to 1 cm and are red to dark brown. They persist, are difficult to treat, and recur if habitual picking is not controlled.

Fig. 2.117 Prurigo nodule is firm, pink, and smooth, with central excoriation.

Treatment

- Medium-potency or high-potency topical corticosteroids (groups II–IV) can be used with plastic-wrap occlusion to enhance penetration and provide a barrier to scratching.
- Corticosteroid-impregnated tape (Cordran) is applied to lesions every day. The covering and occlusion of lesions provides a barrier to the trauma from repeated scratching while medicating the underlying skin.
- Topical superpotent steroids can be applied twice a day to individual lesions for several weeks.
- Intralesional steroid injections (Kenalog 2.5–5 mg/mL) can be given and repeated every 4 to 6 weeks if needed.
- Hypopigmentation in dark skin may occur from such treatment.
- Pramoxine with hydrocortisone (Pramosone ointment) or Sarna lotion may help relieve intense pruritus.

- Oral antihistamine (hydroxyzine, doxepin).
- Light therapy with ultraviolet B, narrow-band ultraviolet B, or psoralen plus ultraviolet A can be considered for severe, generalized cases.
- Cryotherapy is sometimes successful.
- Gabapentin (300–600 mg three times daily) or pregabalin (25 mg three times daily) orally may be useful; caution sedation.
- Excision of individual nodules is rarely performed but is sometimes required.

Discussion

- Complaints of pruritus vary. Few patients claim there is no itching. Scratching is habitual; for most, pruritus is intense.
- Stress is commonly a factor in perpetuating the problem and seems to relate clinically to recurrence or flares. Biofeedback, supportive counseling should be considered.

Pearls

- Exclude medical disease first. A complete skin examination and appropriate laboratory evaluation are critical.
- Do not shy away from discussing stress and anxiety. In some cases, it will be very relevant. Exploring the effect of these important contributors can provide relief and support.
- Providing an alternative ointment to apply can be useful as well—try a bland emollient, such as A&D ointment, zinc oxide ointment, Aquaphor, or petrolatum.
- Intralesional steroid injections and cryotherapy are very effective and are probably the quickest methods for resolving individual lesions.
- Selective serotonin reuptake inhibitors may be helpful. Other therapies for severe cases may include gabapentin, thalidomide, and cyclosporine.

Stasis Dermatitis

Description

- Stasis dermatitis is an eczematous dermatitis of the legs, associated with edema, varicose and dilated veins, and hyperpigmentation.
- Stasis dermatitis is a chronic problem and commonly relapses.

History

- There is often a prior history of deep venous thrombosis, surgery, trauma, or ulceration.
- There is often a family history or personal history of varicose veins.
- The patient complains of heaviness or aching in the leg that is aggravated by prolonged standing or walking.
- The legs are swollen at the end of the day.
- Dermatitis and itching are common findings and can be chronic. Stasis dermatitis can be complicated by contact allergy, especially to medicaments and topical treatments.

Skin Findings

- Dilated and tortuous veins are frequently present on the affected leg. These should be looked for with the patient in a standing position.
- Subacute and chronic eczematous dermatitis appears on the lower legs or surrounding a venous ulcer.
- The dermatitis is obvious and is associated with dry, fissured, erythematous skin.
- The dermatitis can become generalized (id reaction) if the condition persists.
- Edema, brown discoloration (hemosiderosis), erosion, and ulceration are common findings.
- Pruritus is troublesome to the patient; excoriation can potentiate secondary infection.
- White scars on the medial calf indicate previous ulceration. They may have an atrophic, stellate appearance (atrophy blanche).
- Stasis papillomatosis (elephantiasis nostra) and verrucous hyperplasia are found in chronically congested limbs, occurring with local lymphatic disturbances, such as chronic venous insufficiency, primary lymphedema (Milroy's disease), trauma, and recurrent erysipelas.
- Secondary infection with *S. aureus* (impetiginized) is common, especially in excoriated skin.

Laboratory

- In unclear cases, the veins can be studied with color duplex ultrasonography to confirm venous stasis.
- An ankle–brachial index is obtained to check for arterial disease; results of less than 0.8 indicate significant arterial disease.
- In patients with a strong family history or personal history of multiple deep vein thrombosis, the clotting cascade (protein S, protein C, activated protein C resistance, factor V Leiden, cryofibrinogens, and homocysteine level) should be checked.

Treatment

- Cool-water dressings are applied for 10 to 20 minutes twice a day for acute exudative inflammation.
- Groups II to V topical steroids are applied twice a day (cream if acute, and ointment if chronic) for 2 to 3 weeks.
- Domeboro dressings and a course of oral antibiotic (e.g., dicloxacillin, cephalexin) are administered if there is indication of infection.
- For generalized dermatitis (id reaction), an oral steroid is administered with a 3-week taper.

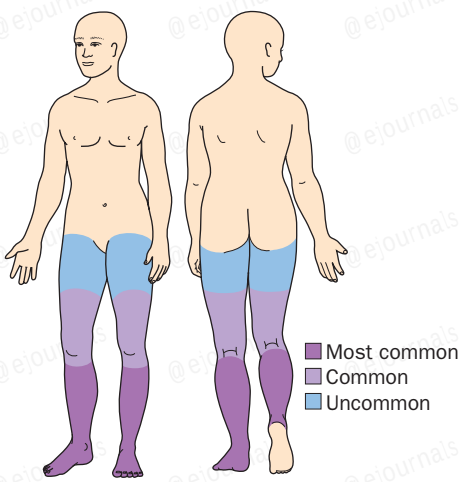

Fig. 2.118 Stasis dermatitis distribution diagram.

- Oral antihistamines (e.g., hydroxyzine) 10 to 25 mg every 4 to 6 hours as needed may help control itching. Caution sedation.
- Lubrication with bland emollients can help alleviate dryness. More Vaseline-like bases, such as plain petrolatum, CeraVe, Aveeno, Cetaphil cream, or Vanicream, are preferable to lotions. Popular moisturizers contain fragrance and preservative ingredients that may contribute to the development of an aggravating contact allergy. Simplify topical applications by using fragrance-free products.
- Compression (20–30 mm Hg) is accomplished with stockings (e.g., Venosan, Sigvaris, or Jobst or Ace wraps).
- More aggressive, prescription or nonprescription compression (30–40 mm Hg at the ankle) worn during the day may be required.
- Venous stasis is a risk factor for development of contact allergy, which can then complicate and perpetuate the eczematous findings

Differential Diagnosis

- Contact dermatitis (especially neomycin, bacitracin, fragrances, preservatives in popular moisturizing lotions, hydrocortisone and other topical corticosteroids; allergic contact dermatitis is commonly associated with stasis dermatitis)
- Cellulitis (sudden pain and increased swelling are clues)
- Tinea corporis (a potassium hydroxide examination of the scale is helpful, especially if there is a moccasin distribution of erythema and scaling on the plantar feet, or onychomycosis)

Pearls

- A careful history often indicates that irritants or potential allergy-causing contactants are being applied by the patient with the intention of healing the skin.
- Simplify the topical management.
- Elevation and compression with graded stockings are mainstays of treatment.
- Topical steroids are very useful for the inflammatory or dermatitis component.
- Patients are often fearful of topical steroids; encourage proper application of topical steroids and use them in ointment base. The patient needs to apply enough, to rub them in well, and to do so for 2 to 3 weeks for acutely eczematous stasis dermatitis.
- If a patient is not agile enough or strong enough to put on compression hose, an Ace wrap can be used successfully to reduce edema. This is applied shortly after rising in the morning and removed at bedtime.

Fig. 2.119 Erythematous papules on the medial aspect of the lower legs in a patient with reticulate starburst superficial varicosities of the ankle. Look for this medial foot and ankle varicosity pattern if stasis dermatitis is suspected.

Fig. 2.120 Stasis dermatitis. This is severe, with marked edema, erythema, scaling, and crusting.

Fig. 2.121 Erythema and scale have extended onto the foot and involve most of the lower leg. A group III topical steroid ointment used for 2 weeks cleared this eruption.

Fig. 2.123 Stasis dermatitis. Erythema, swelling, and itching are present. Patients with stasis dermatitis are at risk for developing contact allergies; thus skin care products should be minimized and chosen carefully from products that do not contain the most common sensitizers.

Fig. 2.122 Stasis dermatitis with ulceration. Breakdown and ulceration of the skin are most common in the medial malleolar region of the lower leg because of recurrent stasis. There is surrounding skin atrophic scarring and hyperpigmentation from prior inflammation.

Venous Leg Ulcers

Description

- A venous leg ulcer is a chronic nonhealing ulcer typically located on the medial aspect of the lower leg in association with chronic venous insufficiency.

History

- Venous leg ulcers often occur in middle-aged and elderly people.
- About 20% of those affected develop ulceration by age 40 years; 13% do so by age 30 years.
- They are more common in women than in men.
- Ulcer formation often occurs suddenly, often after slight trauma.
- Preceding leg injury, phlebitis, obesity, and deep vein thrombosis are also important risk factors.
- Severe pain may indicate other pathologic conditions (e.g., infection or arterial disease).
- Healing is slow, taking weeks or months—even with proper care.
- Venous leg ulcers can be a chronic, recurrent, lifelong problem.

Skin Findings

- Ulcers are typically located in the region of the medial malleolus. They are flat, have sharp or slightly sloping borders, and are typically shallow with a covering of granulation tissue.
- Edema, usually pitting, is common; it improves at night with elevation of the legs.
- Chronic edema, trauma, infection, and inflammation lead to subcutaneous tissue fibrosis in which the skin has a firm, nonpitting, woody quality.
- Ultimately, there is loss of subcutaneous tissue and a decrease in the lower leg circumference.
- Patients complain of aching and swollen legs; the pain is worse with standing and better in the morning.
- Ulcers may be asymptomatic or mildly tender; they do not typically cause severe pain.
- Advanced disease is represented by an "inverted bottle leg"; when the proximal leg swells, the lower leg shrinks.
- Vein varicosities are often prominent.
- The patient may have secondary eczematous dermatitis (stasis dermatitis).
- There is often hyperpigmentation, from either chronic inflammation or capillary leakage, and hemosiderin deposition in the skin of the lower legs.
- The ulcer remains small or may enlarge rapidly without any further trauma.
- Removing crust and debris reveals a moist base with granulation tissue.
- Ulcers are replaced with ivory-white atrophic sclerotic scars (atrophy blanche).

Laboratory

- Color duplex ultrasonography identifies the presence and source of significant venous reflux, an ankle–brachial index is useful in assessing concomitant arterial peripheral vascular disease (the ratio is discussed earlier in the section, Stasis Dermatitis).
- Chronic lesions are excised for biopsy to rule out cancer (basal cell or squamous cell carcinomas) and for tissue culture. A biopsy should be performed if the wound persists longer than 3 months.
- Cultures are not usually helpful; ulcers are often colonized, not infected.
- If infection is a concern, a biopsy should be done and the tissue submitted for bacterial identification and quantification.

Differential Diagnosis

- Most leg ulcers are caused by venous disease. However, the differential diagnosis includes the following:
  - Arterial ulcers
  - Neuropathic ulcers (secondary to diabetes)
  - Infectious ulcers
  - Neoplastic ulcers
  - Metabolic causes
  - Pyoderma gangrenosum
  - Antiphospholipid syndrome or other coagulation disorder
  - Other clotting disorders

Treatment

Control of Chronic Venous Insufficiency

- Proper leg compression can avert recurrence and worsening of the problem.

Fig. 2.124 Recurrent stasis dermatitis. Periodic exacerbations of inflammation are common in areas of stasis. This patient has had recurrent inflammation for years. White sclerotic skin over the ankle is evidence of healed stasis ulcers.

- Elevation of the legs above the heart level for 30 minutes is done three to four times daily and at night.
- Compression is achieved with Ace wraps, graded compression stockings (30–40 mm Hg), or external pneumatic compression devices.
- Multilayer compression bandages are associated with faster healing rates than single-layer bandage systems.
- Unna boots (bandages impregnated with zinc oxide) are also helpful; apply and replace them weekly until the ulcer has resolved.
- The routine use of systemic antibiotics does not increase healing rates.
- Groups III to V topical steroids are used (for 7–14 days) for stasis dermatitis.
- Heavy moisturizing creams in jar form (e.g., Cetaphil, CeraVe, petrolatum, Vanicream, Aveeno cream) protect the skin and help resolve dermatitis. Avoid lotions because they are too drying.
- Neomycin or bacitracin containing topical antibiotics, which may sensitize the skin, should be avoided. Other common contact allergens include preservatives in moisturizing lotions, hydrocortisone, and bacitracin. Avoid these if possible.

Ulcer Therapy

- The crust and exudate are surgically or mechanically débrided.
- Proteolytic enzymes have little benefit in débriding.
- The application of occlusive film promotes rapid healing by suppressing crust formation and enhancing epidermal migration.
- Metronidazole gel (MetroGel) applied before dressing helps decrease odor. Silvadene cream once or twice a day is another good topical option.
- A variety of synthetic dressings are now available.
- Hydrocolloid dressings (e.g., DuoDerm CGF) are effective and easy to use as the initial treatment for uninfected wounds with low to moderate drainage.
- Mepilex is a foam dressing for low to moderate exudative wounds.
- The type of dressing should be changed if healing is slow.
- Exudative and draining ulcers are treated with an absorbent dressing of the calcium alginate group.
- Continuous wet saline dressings can débride the crust in deep ulcers and promote granulation tissue.
- Signs of malnutrition (e.g., a low serum albumin level) should be noted and corrected.
- Vitamin and mineral supplementation should be considered. This includes ascorbic acid (1–2 g daily), zinc sulfate (220 mg three times a day), and vitamin E (200 mg twice a day).
- Skin grafting should be considered for difficult cases; it is most successful when applied to granulation tissue free of exudate and when edema has been controlled.
- Artificially engineered skin substitutes (e.g., Apligraft, Dermagraft) are available

Fig. 2.125 Recurrent inflammation leads to ulceration, and white atrophic scar formation in the area of the medial malleolus. Compression hosiery is helpful to avert this problem in patients with venous stasis, stasis dermatitis, and chronic leg edema.

and should be considered for refractory ulcers.

- Saphenous surgery does not improve ulcer healing but can reduce recurrence rate and ulcer-free time.

When to Refer

- Refer a patient to a dermatologist if patient has a large ulcer size, or for an ulcer of long duration. Refer a patient when ulcer size does not decrease after 1 to 3 months of therapy. Plastic surgeons, dermatologists, and wound care centers provide expertise in wound care.

Pearls

- Make every effort to have your patient understand the importance of good compression measures, such as the daily use of compression stockings. Although difficult at first, often the relief is so great with repeated use that graded compression stockings (Jobst, Sigvaris 25–35 mm Hg at the ankle) are embraced by the patient. These stockings promote more rapid healing and dramatically reduce recurrence.
- An Unna boot is a relatively simple therapy that can provide relief from pain and swelling while healing the ulceration.
- Elevation of the affected leg is an important measure—a patient who must stand all day long may not be able to heal an ulcer. Time off work may be required for healing.
- Venous ulceration can have a major effect on work productivity and quality of life.
- Common infecting organisms are *S. aureus, Pseudomonas aeruginosa,* and beta-hemolytic streptococcus.

Atopic Dermatitis

Description

- Atopic dermatitis is an eczematous eruption that is distressingly pruritic, recurrent, often flexural, and symmetric. There is a familial predisposition.
- Atopic dermatitis generally begins early in life and is characterized by periods of remission and exacerbation. The distribution of affected skin varies with age.

Major Criteria (Four Required for Diagnosis)

- Pruritus
- Young age at onset
- Typical morphology and distribution
- Flexural lichenification and linearity in adults; facial and extensor involvement in infants
- Chronic or chronic and relapsing course
- Personal or family history of atopy (asthma, allergic rhinoconjunctivitis, atopic dermatitis)

Minor (or Less Specific) Features

- Xerosis
- Ichthyosis
- Palmar hyperlinearity
- Keratosis pilaris
- Immediate type I skin test responses
- Dermatitis of the hands and feet
- Cheilitis
- Nipple eczema
- Increased susceptibility to cutaneous infections
- Perifollicular accentuation

History

- The incidence is 7 to 24 per 1000 and seems to be on the rise; it is most common in children.
- About 70% of patients have a family history of one or more of the following: asthma, hay fever, or eczematous dermatitis.
- Aggravating factors include contact irritants and allergens, perspiration, excessive heat, rough fibers (e.g., wool), tight clothing, cool and dry air with no humidity, and emotional stress.
- The role of dust mite and food allergies in cases of severe infantile atopic eczema is controversial.
- Atopic dermatitis becomes less severe in most children when they reach their teenage years. Most children outgrow atopic dermatitis, but some develop chronic relapsing disease, especially of the eyelid and hand, and retroauricular dermatitis.
- Atopic dermatitis seems to result from a vicious cycle of dermatitis associated with elevated T-cell activation, hyperstimulatory Langerhans' cells, defective cell-mediated immunity, and overproduction of immunoglobulin by B cells. Stratum corneum barrier dysfunction and ceramide (an epidermal lipid) deficiency have also been identified as disrupted in atopic skin.

Skin Findings

- Atopic inflammation often begins abruptly with erythema and severe pruritus.
- Typical lesions are red pruritic papules, patches of erythema, and scaling.
- Acute lesions may be oozing and vesicular; subacute lesions are scaly and crusted; and chronic lesions are often dull red, lichenified, and very pruritic.
- Dermatitis distribution varies according to age.

Infantile Phase (2 Months to 2 Years)

- Atopic dermatitis appears on the cheeks, perioral area, and scalp.
- The extensor tops of the feet and the elbows are often involved.
- The lesions are often exudative and weeping.

Childhood Phase (2–12 Years)

- Flexural involvement (antecubital and popliteal fossae, neck, wrists, and ankles) is typical.
- Scratching and chronicity lead to lichenification.

Adult Phase (12 Years to Adult)

- Flexural involvement is common.
- Hand dermatitis may be the only manifestation.
- Dermatitis of the upper eyelids or lips are other frequent findings.
- Atopic dermatitis can be diffuse and patchy on the body.

Fig. 2.126 A common appearance in children with erythema and scaling confined to the cheeks and sparing the perioral and paranasal area.

Fig. 2.127 Generalized infantile atopic dermatitis sparing the diaper area, which keeps the skin hydrated and protected from scratching.

- Associated findings are dry skin, ichthyosis vulgaris, and keratosis pilaris.

Complications

- Lesions are frequently colonized with *S. aureus;* secondary infection resulting in another flare of dermatitis or persistence is common.
- Increased susceptibility to viral infections (herpes simplex, molluscum contagiosum, cutaneous fungal infections) is frequent.
- Hypopigmentation and hyperpigmentation may result from previous inflammation.
- Emotional and behavior problems may be frequent in children affected by moderate to severe disease.

Nonskin Findings

- Often, there is a personal or family history of asthma, hay fever, or seasonal rhinitis.

Laboratory

- Laboratory studies are not routinely indicated or performed.
- Culture and sensitivity testing of crusted or oozing lesions is performed if bacterial superinfection is suspected.
- Elevated immunoglobulin E levels (>200 international units/mL) occur in approximately 80% to 90% of patients.
- The incidence of eosinophilia correlates roughly with disease activity.
- Routine allergy testing, dietary testing, and environmental or dietary manipulation are often performed in severe and refractory cases.
- Patch testing should be considered if the pattern of dermatitis changes or the condition becomes more refractory to treatment.
- Children with severe atopic dermatitis may have food allergies. Evaluation and elimination of suspected foods under medical supervision can be helpful in some cases. Food allergy is rarely a problem for adults with atopic eczema.

Differential Diagnosis

- Contact dermatitis (irritant or allergic types)
- Nummular eczema and seborrheic dermatitis
- Scabies (consider in new-onset eczematous disease)
- Cutaneous T-cell lymphoma (consider especially in adults with refractory disease)
- Tinea infections (potassium hydroxide examination of scale is helpful)

- Uncommon: congenital disorders, metabolic disorders (zinc deficiency), immune deficiency disorders (Wiskott–Aldrich syndrome, hyperimmunoglobulinemia E syndrome, severe combined immunodeficiency, Netherton's syndrome)

Treatment

- The skin barrier should be restored and preserved.
- Bland emollients, such as Vaseline petroleum, should be used. A plain, thick, greasy moisturizer cream (Vaseline, Aquaphor, Aveeno, Cetaphil, and Vanicream) without fragrances or common sensitizing preservatives is ideal and is preferable to commonly available lotions or creams. Newer moisturizers containing a ceramide dominant lipid (CeraVe) have a modest effect in alleviating disease activity.
- Inflammation and infection should be controlled or eliminated.
- Topical corticosteroids of appropriate strength for the patient's age and the affected area are applied twice daily to inflamed skin for 10 to 21 days.
- Topical immune modulators: tacrolimus (Protopic) ointment 0.03% for children aged 2 to 15 years and 0.03% and 0.1% for adults, or pimecrolimus (Elidel) cream 1% twice daily for short-term and intermittent long-term therapy are effective topical immune modulators. Their use can avoid the adverse effects associated with chronic topical steroids. They are especially helpful for atopic dermatitis of the face, eyelids, or areas of limited involvement.
- Oral antibiotics, such as dicloxacillin and cephalexin (Keflex), are administered for secondary infection. Topical Mupirocin (Bactroban) cream twice daily for 5 days may be helpful if infection is limited.
- For acute lesions and severe flares, wet dressings with Burow's solution are applied for 20 minutes two or three times a day, followed by the application of a topical steroid.
- If lesions suddenly become exquisitely tender with small ulcerations, consider herpes simplex infection complicating atopic eczema (eczema herpeticum).
- Dilute bleach baths two to three times per week can help decrease bacterial eczema triggers. Use ½ cup of regular strength (6%) bleach in a full tub of water or ¼ cup of bleach in a half tub of water. For infants and toddlers, use 1 teaspoon bleach per gallon of water in bath. Soak 5 to 10 minutes, pat dry after bath, and moisturize skin.
- Aggravating factors must be eliminated or controlled.
- Excessive sweating, which is irritating to the skin, should be avoided.
- Soft, light cotton clothing is best; wool or other coarse fibers are to be avoided.
- The environment should be cool and well ventilated.
- Stress reduction techniques may be helpful.
- Pruritus must be controlled.
- Oral antihistamines with sedative effects are helpful, such as diphenhydramine (Benadryl), hydroxyzine (Atarax), and doxepin, especially at night to allow more restful sleep.
- A dermatologist should be consulted for the management of severe, refractory disease.

Severe Atopic Dermatitis

- A *short* course of oral corticosteroids can break the cycle of inflammation.
- Tacrolimus ointment (Protopic) and pimecrolimus cream (Elidel) are both effective when applied twice a day but may not work as fast as topical steroids. They should be used on limited skin surface areas.
- Consider hospitalization for rest, environmental control, and stress reduction, and wet dressings two times a day followed by the application of a medium-potency topical steroid.
- A medium-potency topical steroid with vinyl-suit occlusion can be applied for 2 hours twice a day for 1 to 2 weeks.
- Ultraviolet light therapy includes broad- or narrow-band ultraviolet B, and psoralen plus ultraviolet A.
- Other immunomodulating therapeutic options for severe refractory atopic eczema include oral cyclosporine, azathioprine, low-dose methotrexate, and interferon gamma.

- Immunotherapy: Dupilumab was recently approved in the United States and is a major breakthrough in the treatment of severe atopic dermatitis. This monoclonal antibody blocks interleukin-4 and interleukin-13 signaling. Administered as two subcutaneous injections for the first dose, and one injection of 300 mg every 2 weeks thereafter. Possible adverse effects are injection site reactions and conjunctivitis (10%).

Pearls

- Control aggravating external environmental factors.
- Win patient compliance by education, support, empathy, and good listening. Schedule follow-up visits—even if just for support.
- Be specific with your treatment recommendations.
- It is wise to emphasize that atopic dermatitis cannot be cured, but it can be managed with good care plans. Consultation with a specialist can help in severe or refractory cases.

Fig. 2.128 Flexural involvement is seen in atopic dermatitis. The popliteal fossae and antecubital fossae are classical areas of involvement. Skin is often very pruritic and lichenified.

Fig. 2.130 Atopic dermatitis. This is the classical appearance of confluent papules forming plaques in the antecubital fossa.

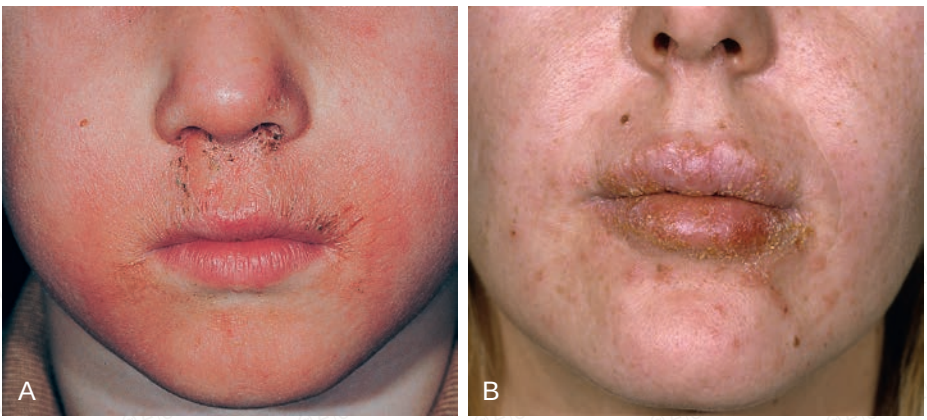

Fig. 2.129 Atopic eczema in the perioral and lip area is common in both childhood and adult disease.

Fig. 2.131 Hand dermatitis is common in patients with atopic dermatitis. Irritants and wet work are best avoided.

Fig. 2.133 Accentuation of the skin creases on the palms (hyperlinear creases) is a distinctive sign of the atopic diathesis.

Fig. 2.132 Erythema and scale on the cheeks are one of the most common presentations for atopic dermatitis in infants. Crusting suggests secondary infection with staphylococci.

Fig. 2.134 Atopic dermatitis. The mother was afraid to use topical steroids. Washing and scratching caused the inflammation to spread over a wide area. Antistaphylococcal oral antibiotics, followed by application of a group VI topical steroid ointment, cleared the eczema. Pimecrolimus cream (Elidel) was used to prevent recurrence.

Fig. 2.135 Severe, widespread atopic dermatitis. The discomfort of itching is unbearable.

Autosomal Dominant Ichthyosis Vulgaris

Description

- Dominant ichthyosis vulgaris is a disorder of keratinization characterized by dry, rectangular scales resembling a cracked pavement; these scales appear most prominently on the extensor extremities.
- It is associated with the atopic diathesis in 50% of cases.

History

- The onset is in early to middle childhood.
- The condition may improve with age or may persist throughout life.
- The scales are more noticeable and often pruritic in the winter, when the humidity is low.
- Ichthyosis vulgaris is autosomal dominant; 1 in 300 have the disorder.
- It may be confused clinically with X-linked ichthyosis.

Skin Findings

- Findings are often mild.
- Dry, small, rectangular scales appear on the extensor extremities.
- The lower extremities, particularly the anterior shins, are often more noticeably affected.
- Affected skin has the appearance of cracked pavement or fish scales.
- This condition characteristically spares the flexor surfaces.
- It is usually asymptomatic but may become pruritic or chapped in the winter.
- Palmar creases may be accentuated.
- Keratosis pilaris may also be present.
- Scaling rarely involves the entire cutaneous surface.
- Scaling of the skin results from the retention of scale rather than increased proliferation.
- The condition may result from a defect in the synthesis of the epidermal proteins profilaggrin and filaggrin.

Laboratory

- No tests are routinely indicated, unless there is a question of X-linked ichthyosis.
- Skin biopsy is rarely performed; when performed, it shows in a subset of patients a decreased or an absent granular layer.

Differential Diagnosis

- Dry skin
- Acquired ichthyosis (more sudden and later onset, generalized, as a manifestation of systemic disease—that is, infection with the immunodeficiency virus, sarcoidosis, malignancy, drugs, metabolic diseases, autoimmune disease, and in bone marrow transplant recipients with a history of chronic graft-versus-host disease)
- X-linked ichthyosis (affected males have deficient steroid sulfatase activity; large scales are a dirty brown color; flexures may be involved, although usually spared; a fluorescence in situ hybridization test is performed on fibroblasts, keratinocytes, and lymphocytes and is a sensitive test for X-linked ichthyosis). Deficiency of placental steroid sulfates may result in delayed progression of labor.

Treatment

- Ichthyosis vulgaris often improves with age; infrequently, it resolves completely.
- Increased environmental humidity and warmth often result in resolution or improvement.

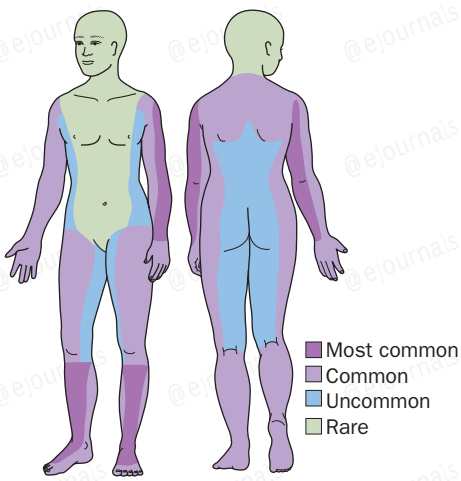

Fig. 2.136 Dominant ichthyosis vulgaris distribution diagram.

Fig. 2.137 Dominant ichthyosis vulgaris. White, translucent quadrangular squares on the extensor aspects of the arms and legs. This form is significantly associated with atopy.

Fig. 2.138 Dominant ichthyosis is a disorder of keratinization characterized by the development of dry, rectangular scales. The skin on this patient's lower leg shows features of ichthyosis and asteatotic eczema.

- Regular application of moisturizing cream or lotion decreases pruritus and improves skin appearance.
- The optimal time for applying moisturizer is immediately after bathing and hydrating the skin.
- Emollients containing lactic acid, cholesterol, or alpha-hydroxy acids are helpful for treating severe dryness and scaling. Alpha-hydroxy acids can sting.
- Ammonium lactate 12% (Amlactin) lotion or cream is very effective when applied daily.

Pearls

- Clues to the differential diagnosis of X-linked ichthyosis include cryptorchidism in affected patients and a birth history of delayed labor. Half of affected males and female carriers develop comma-shaped corneal opacities.

Keratosis Pilaris

Description

- Keratosis pilaris consists of rough, monomorphic, tiny, follicle-based scaling papules most commonly on the posterolateral aspects of the upper arms but occasionally more widespread, including the anterior and lateral thighs and the buttocks.
- It results from mild follicular plugging and perifollicular inflammation.

History

- Keratosis pilaris is very common in young children, peaking in adolescence.
- It is probably more common in atopic individuals.
- It is usually asymptomatic but may be somewhat pruritic.
- Treatment is often sought for a troubling cosmetic appearance.
- The unusual adult diffuse pattern persists indefinitely.

Skin Findings

- Small, pinpoint follicular papules, and occasionally pustules, remain in the same areas for years.
- A red halo appears at the periphery of the keratotic papule.
- The skin feels rough, like sandpaper.
- Lesions most commonly appear on the posterolateral upper arms and anterior and lateral thighs. Occasionally, the condition is generalized and appears on the trunk, extensor arms, and legs.

Laboratory

- No laboratory tests are necessary.

Differential Diagnosis

- Acne (facial lesions may be confused with it; uniform small size and association with dry skin and chapping differentiate keratosis pilaris from pustular acne)

Treatment

- Many patients seek treatment for cosmesis because most often the lesions are asymptomatic.
- Keratosis pilaris often improves or resolves by adulthood.
- Scratching, wearing tight-fitting clothing, or undergoing treatment with abrasive washes or gritty scrubs may aggravate the condition.
- Tretinoin (Retin-A) may induce temporary improvement, but irritation is usually unacceptable.
- Lac-Hydrin cream 12% or lotion 12% twice a day can reduce roughness and improve appearance.
- Low-potency topical steroids may be used in limited courses to temporarily reduce the redness but should not be used on a long-term basis.
- The recognition of keratosis pilaris helps avoid inappropriate treatment.

Pearls

- Keratosis pilaris is common on the face of children and is frequently confused with acne.

- Treatment is often desired because of the visible typical location of keratosis pilaris on the extensor upper arms and thighs. Otherwise, the condition is generally asymptomatic.
- Use of an emollient daily can lessen the appearance and inflammation of keratosis pilaris, which can be especially apparent during winter months.

Fig. 2.139 The upper outer arm is the most common location for these erythematous, rough, nutmeg-grater–like papules of keratosis pilaris. The main complaint of patients is the altered skin appearance, which some consider unsightly.

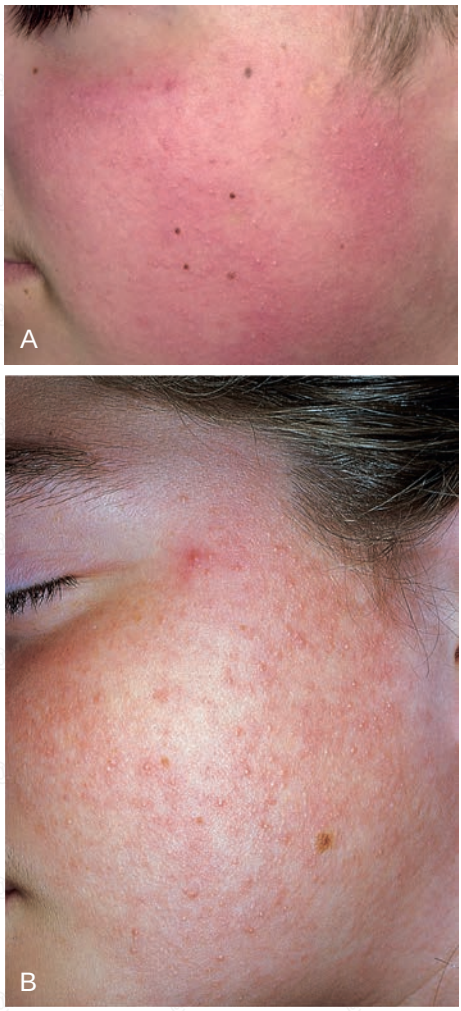

Fig. 2.140 Keratosis pilaris can occur on the face, most commonly the lateral cheeks in children and adolescents. The intensity of erythema is variable.

Pityriasis Alba

Description

- Asymptomatic, hypopigmented, slightly elevated, fine, scaling patches with indistinct borders, typically on the lateral cheeks.
- Pityriasis alba affects the lateral cheeks, lateral upper arms, and thighs; it occurs more frequently in young children and usually resolves by early adulthood.

History

- Pityriasis alba is asymptomatic.
- Children and young adults are affected.
- There is no history of prior rash, trauma, or inflammation.
- Affected individuals are often atopic.
- Loss of pigment is often more noticeable and distressing in darkly pigmented people.

Skin Findings

- The white macules are round to oval and vary in size; they are generally 2 to 4 cm in diameter.
- A fine surface scale may be seen on close inspection.
- Lesions are most common on the lateral cheeks, lateral upper arms, and thighs.
- The condition is more obvious in the summer, and in darker skin types, when affected skin does not tan.

Laboratory

- A potassium hydroxide examination of the fine scale is negative.

Differential Diagnosis

- Eczematous dermatitis
- Tinea versicolor (rare on the face)
- Vitiligo (more sharply demarcated, often over joints, symmetric, and more widespread)
- Chemical leukoderma
- Hypopigmented cutaneous T-cell lymphoma (rare, more often truncal)

Treatment

- Usually no treatment is recommended because the problem is benign and self-resolving. Emollient use every day may be helpful.
- The patient should be reassured that the loss of pigment is not permanent.
- Hypopigmentation usually fades with time.
- Hydrocortisone cream or ointment 1% applied for a limited time (a few weeks) on affected skin may help the patients who are most distressed by the pigment irregularity.

Pearls

- Hypopigmented round spots are a common occurrence on the faces of atopic children.
- The superficial hypopigmented plaques become scaly and inflamed as the dry winter months progress.
- Reassurance and the application of moisturizers usually is sufficient.
- Application of a groups VI to VII topical steroid for a few days will control mild inflammation.

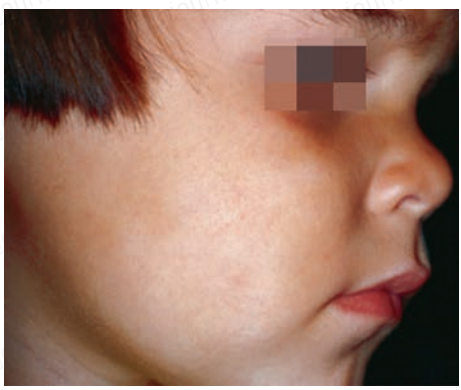

Fig. 2.141 Pityriasis alba on the face is a common finding. Parents are concerned about the cosmetic appearance. They are reassured when informed that the white spots will disappear in time.

Fig. 2.142 Hypopigmented patches on the lateral face consistent with pityriasis alba.

Fig. 2.143 Hypopigmented patches on the arm in a patient with pityriasis alba. The differential diagnosis includes tine versicolor, vitiligo, and hypopigmented cutaneous T-cell lymphoma.

Fig. 2.144 Faint hypopigmented patches on the upper extensor arms. This is most likely pityriasis alba. If extensive or expanding patches, the differential diagnosis should include hypopigmented cutaneous T-cell lymphoma.

Urticaria 3

M. Shane Chapman

Acute Urticaria

Description

- Urticaria, or hives, is divided into acute and chronic forms based on the duration of the hives.
- Acute urticaria, by definition, lasts for less than 6 weeks, whereas chronic urticaria lasts more than 6 weeks.
- Urticaria is a common, pruritic, distinctive reaction pattern.
- Transient, migratory, edematous, pink to red plaques vary in size and shape. Individual lesions typically last less than 24 hours.

History

- The etiology or trigger of most cases of urticaria is undetermined.
- Acute urticaria may occur at any age.
- It is more common in atopic individuals and is notoriously intensely pruritic.
- Hives are caused by histamine release induced by allergens or triggers, such as medications, injections, foods, or airborne allergens.
- Angioedema is a histologically deeper variant of urticaria, is somewhat less pruritic, and more commonly affects mucosa.

Skin Findings

- The edematous plaques are red or pink to flesh-colored and may be surrounded by a white or pink halo.
- Individual lesions vary in size, from 2 mm papules to 3 cm or larger wheals.
- They are typically round or oval in shape and can become polycyclic and confluent.
- The plaques change size and shape and migrate and regress over time.
- This is a dynamic process, and new lesions evolve as old ones resolve.
- Rarely, bullae or purpuric lesions appear with intense swelling.
- The distribution is usually generalized and haphazard.
- Linear lesions suggest dermatographism, a type of hive created by scratching.

Laboratory and Testing

- There are no reliable routine studies for diagnostic confirmation of urticaria.
- Biopsy is usually not required for diagnosis of acute hives.
- If urticarial vasculitis is suspected, a biopsy can help confirm this diagnosis.
- For the most part, urticaria is a clinical diagnosis.

Differential Diagnosis

- Medication allergy or eruption
- Viral exanthem
- Bite reaction (papular urticaria)
- Bullous pemphigoid (early stages)
- Urticarial vasculitis
- Hereditary angioedema (mucosal involvement)

Treatment

- All suspected triggers, such as medications, food, inhalants, and injections, should be discontinued.
- Antihistamines are typically administered initially: sedating type 1 histamine receptor antagonists (e.g., hydroxyzine [10 mg, 25 mg, 50 mg, 100 mg] 10 mg/5 mL) can be helpful but are limited by drowsiness. They are administered every 4 or 6 hours.
- The nonsedating antihistamines (e.g., cetirizine 5 mg, 10 mg) are also helpful but may have to be used in combination with sedating histamine-1 (H_1)-blocking antihistamines. They are taken once every 24 hours but may be taken twice a day in difficult cases.
- Prednisone is rapidly effective and can be given periodically; it may work in patients

whose condition is difficult to control with antihistamines.
- Combinations of H_1 and H_2 blockers is another treatment strategy.
- Doxepin, a tricyclic antidepressant and an antihistamine, can be used in recalcitrant cases.
- Epinephrine is administered for extensive, severe cases, but the effects are short-lived.
- Cool, soothing baths can be suggested.
- Hot showers should be avoided because they worsen the pruritus afterward.
- Topical steroids are generally not effective.

Pearls

- The etiology may not be discovered in most cases.
- By definition, acute urticaria resolves within 6 weeks, with or without treatment.
- Individual hive or urticarial lesions migrate, change in shape, and typically resolve within 24 hours.

Fig. 3.2 Acute urticaria. Urticaria resolves spontaneously in less than 14 days in most patients. It persists for months and sometimes years in about 5% of patients. These lesions have a clear center, and the surrounding skin is diffusely red and less swollen.

Fig. 3.1 Acute urticaria. Large circumscribed, raised, edematous, red plaques. The itch can be intense. Lesions range from a few to numerous and vary in size and configuration.

Fig. 3.3 Acute urticaria. Lesions occur on any skin surface, including the palms, soles, and face. They appear in many forms, and each lesion lasts 12 to 24 hours. The most characteristic presentation is a red, raised plaque with central clearing, surrounded by a faint white halo. When confluent, they become polycyclic.

Chronic Urticaria

Description

- Chronic urticaria is defined as urticaria or hives of the skin lasting more than 6 weeks.
- This variation of hives requires investigation to the etiology of the urticaria, which can require significant workup.

History

- Chronic urticaria is usually easily diagnosed but presents a treatment and management dilemma.
- The underlying cause of chronic urticaria is discovered in only 5% to 25% of cases.
- People of all ages are affected, but the highest incidence is in young adults.
- The course of the disease is unpredictable, and the disease can last months or years.
- Patients should be evaluated for the "five I's":
  - Ingestants (most common): medications, foods, additives.
  - Inhalants: dust, feather, pollen.
  - Injectants: vaccines, drugs, stings, bites.
  - Infections: bacterial, viral, fungal, parasitic.

Fig. 3.4 Chronic urticaria is common, occurring in up to 25% to 50% of the population. People of all ages are affected, but the highest incidence is in young adults.

Fig. 3.5 Chronic urticarial. Lesions may become confluent and sometimes cover an entire extremity.

  - Internal diseases: chronic infections, thyroid disease, lupus erythematosus, occult cancer (rare).

Skin Findings

- Clinically, chronic and acute urticarias are indistinguishable.
- The edematous wheals and plaques are pink to red in color, figurate, and annular, with central clearing.
- Lesions vary in size from just millimeters to areas that can cover an entire hand.
- These plaques can be coalescing and polycyclic, change in size and shape over time, and migrate.
- Individual lesions resolve within 24 hours, whereas new lesions continue to appear.

Laboratory and Testing

- The cause may be unclear after routine history and physical examination.
- Laboratory tests may be ordered but are rarely helpful.
- Tests to consider include a complete blood count, sinus radiographs to evaluate for sinusitis, dental radiographs to evaluate for an occult dental abscess, rapid streptococcal test or pharyngeal culture, and a thyroid-stimulating hormone and thyroid microsomal antibody test for autoimmune thyroid disease.

- Other tests may be acquired slowly based on the physical signs and symptoms of the patient.

Differential Diagnosis

- Physical urticaria
- Erythema multiforme
- Urticarial vasculitis
- Bullous pemphigoid (early stages)

Treatment

- Antihistamines (H_1 type) are prescribed initially, most commonly diphenhydramine and hydroxyzine.
- They are the backbone of therapy for acute and chronic urticaria.
- Hydroxyzine 10 to 25 mg or diphenhydramine 25 to 50 mg can be administered every 4 hours, up to 100 mg every 4 hours as needed, but can be sedating.
- Nonsedating antihistamines (H_1 type) should be considered for daytime use and include cetirizine, desloratadine, and fexofenadine.
- H_1-blocking antihistamines may be combined with H_2-blocking antihistamines, such as cimetidine 400 mg twice daily or ranitidine 150 mg twice daily.
- Doxepin, a tricyclic antidepressant and antihistamine, can be prescribed in difficult cases.
- Oral steroids are a second line of treatment for hives; however, their use for chronic urticaria is controversial and sometimes detrimental, especially if high doses are required.
- Epinephrine is rarely required; the effect is short-lived.

Fig. 3.6 Chronic urticarial. The presentation is highly variable. Small lesions expand to larger plaques and become polycyclic.

Fig. 3.7 Chronic urticarial. Some lesions can be slightly elevated and wheal-like, in various shapes. Thicker plaques tend to have a uniform color.

Fig. 3.8 Chronic urticarial. Some patients with extensive involvement have systemic symptoms, such as shortness of breath, wheezing, nausea, abdominal pain, diarrhea, and headache.

- Empiric antibiotic therapy may be tried if an occult infection, such as a tooth abscess, or sinusitis is suspected.
- Despite aggressive therapy, many cases of chronic urticaria persist indefinitely.

Pearls

- Individual urticarial lesions are recurrent, migratory, and pruritic but tend to resolve in a 24-hour period while new lesions appear.
- Some cases of chronic urticaria may be recurrent and not resolve after several months or years, with an unknown cause.
- Urticarial vasculitis is a systemic disease that may be related to lupus erythematosus, which mimics chronic urticaria but differs in that it leaves purpuric patches. Diagnosis is made by biopsy, which shows a vasculitis within the urticarial lesion.
- Early bullous pemphigoid may present with urticarial plaques before bullae formation.
- Rarely, an underlying occult cancer can be associated with chronic urticaria.

Physical Urticaria

Description

- Physical urticaria is a brief attack of urticaria or hives induced by physical stimuli, such as scratching, pressure, vibration, heat, cold, and ultraviolet light.
- The episode may be short-lived but may recur with recurrent stimulation.

History

- The major distinguishing feature is that these eruptions are brief and usually self-limited.
- Most of these episodes of urticaria last 1 to 6 hours.
- Dermatographism is the most common physical urticaria, which is when hives are produced by rubbing and stroking the skin.
- This entity can be triggered by viral infection, antibiotic therapy, or emotional upset, although the cause is usually not determined.
- Pressure urticaria occurs 4 to 6 hours after a pressure stimulus and may last from 8 to 72 hours. Deep burning or painful swelling occurs. The hands, feet, trunk, buttocks, lips, and face are commonly affected. Lesions are induced by standing, by walking, by wearing tight garments, or by sitting on a hard surface for long time. This condition can be disabling for those performing manual labor.
- Cholinergic urticaria is a variant of hives that begins within 1 to 20 minutes of overheating from exercise, exposure to heat, or emotional stress. It may last for minutes to hours.
- It is more common in young patients and tends to be chronic.
- Cold urticaria occurs with a sudden drop in air temperature or exposure to cold water. This condition can be initiated after infection, drug therapy, or emotional stress.
- In solar urticaria, hives occur minutes after exposure to ultraviolet light and disappear in about 1 hour. Several different wavelengths of ultraviolet light cause solar urticaria, and some may consider this to be a variant of polymorphous light eruption. In most, this condition is persistent.

Skin Findings

- The physical urticarias may present with pruritic, linear wheals after rubbing or scratching, which is the definition of *dermatographism*.
- This test can be performed in the office by stroking a pencil eraser or cotton swab on the forearm.
- Repeated deep swelling at sites of prolonged pressure is a clue to the diagnosis of pressure urticaria.
- Annular hive lesions, 2 to 4 mm in diameter, surrounded by extensive red flare are characteristic of cholinergic urticaria.
- Cold and solar urticarias are similar in clinical appearance to other forms of urticaria and are generally diagnosed by a history of exposure.

Tests

- The diagnosis is usually suspected by the clinical examination and history and confirmed by one of several simple office tests.
- For dermatographism or physical urticaria, a tongue blade or cotton swab stroked firmly across the forearm or back produces a linear wheal-like lesion within minutes.
- In pressure urticaria, testing with localized pressure points can usually confirm the diagnosis.
- In cholinergic urticaria, the patient runs in place or uses an exercise bicycle for 10 to 15 minutes. Then the patient is observed for up to 1 hour to detect typical papular hives.
- In cold urticaria, hives are induced with an ice pack or an ice cube held against the skin for 1 to 5 minutes.
- In solar urticaria, phototesting with ultraviolet A, ultraviolet B, and visible light identifies the wavelengths that produce the hives.

Differential Diagnosis

- Polymorphous light eruption and lupus erythematosus can be confused with solar urticaria
- Although controversial, some think all three of these entities are related

Treatment

- In dermatographism, treatment is often unnecessary. Symptomatic dermatographism is treated with antihistamines, such as hydroxyzine and diphenhydramine.
- The conditions of many patients are controlled for long periods with very low doses of antihistamines, such as hydroxyzine.
- Long-acting, nonsedating antihistamines (cetirizine, desloratadine, and fexofenadine) can also be effective.
- In cholinergic urticaria, limiting strenuous exercise or administering hydroxyzine before exercise can be helpful.
- In cold urticaria, the patient should be protected from sudden decreases in temperature; and cyproheptadine, another short-acting antihistamine, can be effective but sedating. The dosage is adjusted to control symptoms.
- In solar urticaria, antihistamines can be employed, but sunscreens and vigorous sun avoidance should be recommended. For some patients, small, incremental increases in ultraviolet light may be helpful.

Fig. 3.9 Dermatographism is the most common form of physical urticaria. Scratching produces a linear wheal that fades in 15 to 60 minutes. Itching is mild to intense. The skin should be stroked in any patient who complains that scratching creates itching and swelling.

Fig. 3.10 Dermatographism. Linear hives that are created by scratching, rubbing, and digging the skin.

Angioedema

Description

- Angioedema is an acute or chronic hive-like swelling in the deeper subcutaneous tissue of the skin and mucosa.
- Hereditary angioedema is characterized by recurrent episodes of intense edema and swelling in several locations in people who are genetically predisposed.

History

- Hives and angioedema commonly occur simultaneously, but not always.
- The deeper reaction of angioedema produces a more diffuse swelling, which can be dramatic.
- Itching is usually absent, but burning and painful swelling are typical.
- The lips, palms, soles, limbs, trunk, and genitalia are most commonly affected.
- Involvement of the gastrointestinal and respiratory tracts produces dysphagia, dyspnea, colicky abdominal pain, and attacks of vomiting and diarrhea.
- There are two forms of angioedema: acute and chronic.
- In acute angioedema, there is a severe allergic type 1 immediate hypersensitivity immunoglobulin E–mediated reaction that is usually self-limited.
- Identification and removal of the offending agent, when known (e.g., medications, contrast dyes, foods) is usually curative. Most of these acute attacks resolve within 24 to 48 hours.
- The etiology of most cases of chronic angioedema is unknown.
- The condition is most common in 40- to 50-year-old women.
- The pattern of recurrence is unpredictable, and episodes can occur for 5 or more years.
- Late-onset, recurrent angioedema may indicate an acquired deficiency of C1q esterase inhibitor.
- Two types of acquired angioedema are described. One form is associated with malignancy, usually B-cell lineage, and the other is defined by the presence of an autoantibody directed against the C1 inhibitor molecule. Both are very rare but, when present, require a search for the underlying etiology, especially occult malignancy.
- Hereditary angioedema is an autosomal dominant variant of the disease, of two or three types, all with similar signs and symptoms (including acute and chronic angioedema).
- Hereditary angioedema may result from known or unknown triggers and can affect the skin, mucosa, and visceral organs, typically with massive edema.

Skin Symptoms

- The reaction is similar to that of hives, but in angioedema, there is also deeper swelling of the subcutaneous tissues of the skin and mucosa.
- The clinical appearance tends to be more dramatic than typical hives and can cause disfigurement to the point at which the patient is unrecognizable.
- Occasionally, eyes can be swollen shut; oral mucosa can be so edematous that phonation can be affected.
- In hereditary angioedema, the gastrointestinal tract and upper airway can be involved in addition to the skin and mucosa, and can be life-threatening.

Laboratory and Testing

- Thyroid microsomal and thyroglobulin antibodies are present in some patients with chronic angioedema.

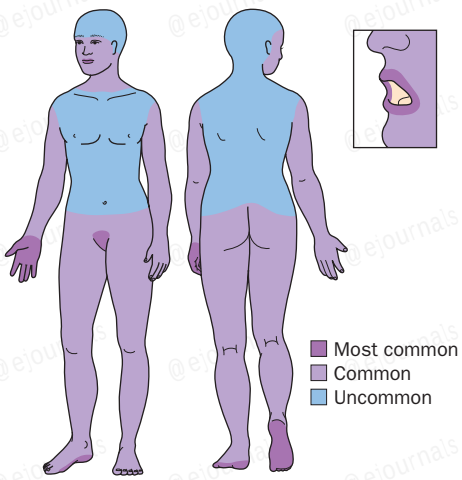

Fig. 3.11 Angioedema distribution diagram.

- Patients with acquired C1-inhibitor deficiency have low levels or absence of functional C1-inhibitor activity and low levels of CH_{50}, C1q, C1, C4, and C2.
- Quantitative and functional analysis of C1 esterase inhibitor and C4 should be performed when hereditary angioedema is suspected.

Treatment

- Acute severe attacks are treated with epinephrine and high dosages of antihistamines.
- An epinephrine autoinjector (EpiPen) should be considered for patients who experience recurrent severe reactions.
- Affected patients should wear a medical alert bracelet that identifies the diagnosis and risk.
- For chronic relapsing courses of the disease, antihistamines such as hydroxyzine can be used quickly to slow reactions.
- Systemic corticosteroids may be required for suppression in some severe, recalcitrant cases.
- The use of levothyroxine should be considered if patients are hypothyroid.
- For hereditary angioedema, intravenous purified C1 esterase inhibitor concentrate should be given if available.
- Intravenous fresh frozen plasma can also be useful.
- Steroids, antihistamines, and epinephrine and other agents can be helpful adjuncts.

Pearls

- Angioedema can affect the face, lips, palms, soles, or a portion of an extremity.
- The edema may become confluent and cover wide areas. The color is uniform, whereas hives are generalized and may vary in color.
- Angioedema is a hive-like swelling caused by increased vascular permeability in the subcutaneous tissue of the skin and mucosa.
- Hives and angioedema may occur simultaneously.

Fig. 3.12 Angioedema affects the face, lips, palms, soles, extremities, and trunk. Angioedema may become confluent and cover wide areas. The color is uniform.

Fig. 3.13 Angioedema is a hive-like swelling caused by increased vascular permeability in the subcutaneous tissue of the skin and mucosa. Hives and angioedema may occur simultaneously. Itching is usually absent. Symptoms consist of burning and painful swelling.

Fig. 3.14 Angioedema. Urticarial plaques are confluent and cover wide areas.

Mastocytosis (Urticaria Pigmentosa)

Description

- Cutaneous mastocytosis, or urticaria pigmentosa, is a rare disease in which the skin is excessively infiltrated by mast cells.
- There are several clinical presentations, but the childhood or pediatric cutaneous, or urticaria pigmentosa, form is the most common.
- Other variants of cutaneous mastocytosis and mast cell disease include telangiectasia macularis eruptiva perstans (TMEP), solitary mastocytoma, and diffuse cutaneous mastocytosis.
- There are more severe systemic variants of mast cell disease, including mast cell leukemia, but these can present differently and are rare.

History

- The cause of mastocytosis is unknown.
- The incidence of cutaneous mastocytosis is 1 in 1000 to 8000 live births.
- The onset is between birth and 2 years of age in about 50% of cases.
- Mastocytosis is usually confined to the skin in young children.
- Adults are more likely to develop systemic forms of mast cell disease.
- Typically, the condition improves gradually and usually clears spontaneously by puberty.
- Mast cell disease that begins after age 10 years may persist for life.
- When this disease is systemic, the gastrointestinal tract and the skeletal system are most commonly involved, and there can be associated mast cell leukemia.
- When large numbers of mast cell lesions are present, pruritus can be severe and difficult to treat.

Skin Findings

- There are two main types of mastocytosis: localized and generalized.
- The most common presentation is pediatric-onset with a localized cutaneous disease.
- Skin findings consist of red-brown, slightly elevated, nonblanchable macules and patches, averaging in 5 mm to 2 cm diameter.
- Macules and patches of mastocytosis lesions, may occur in small groups or be generalized on the trunk and extremities.
- The macules and slightly elevated patches are often dismissed as variations of pigmentation or café-au-lait macules.
- A larger, nodular and solitary variant is called a *mastocytoma*.
- Erythema and blisters induced from scratching are common in the first 2 years of life.
- Darier's sign is a characteristic finding and is induced by stroking any lesion, which induces intense erythema and a wheal response.
- This reaction (Darier's sign) is the hallmark of urticaria pigmentosa.

Laboratory and Testing

- A skin biopsy can be very helpful, but special stains may be required.
- Metachromatic stains, such as Giemsa and toluidine blue, stain cytoplasmic mast cell granules deep blue.

Fig. 3.15 Mastocytosis. A large, solitary, >1 cm red-brown indurated nodule in an infant that develops a wheal with gentle stroking, characteristic of a mastocytoma.

Fig. 3.16 Mastocytosis. A positive Darier's sign of the mastocytoma lesion in Fig. 3.15.

Fig. 3.17 Mastocytosis. Darier's sign is characterized by the development of an erythematous, edematous wheal at the site of palpation or stroking of a mastocytosis lesion, about 30 to 60 seconds after stroking.

Fig. 3.18 Mastocytosis. Small 2- to 3-mm pigmented macules over the back of this adult, which are characteristic of the urticaria pigmentosa variant of mastocytosis.

Fig. 3.19 Mastocytosis. Small 2- to 3-mm red-brown macules generalized over the trunk of this infant, which become inflamed and erythematous with gentle stroking and palpation. Slight hyperpigmentation may persist after the inflammation resolves.

- Sparse numbers of mast cells are normally present in skin, but significantly increased numbers of mast cells around vessels are diagnostic.
- Urinary *N*-methylhistamine (the major metabolite of histamine) is used as a measure of systemic disease.

Differential Diagnosis

- Urticaria
- Dermatographism
- Bite reaction
- Café-au-lait macules
- Congenital pigment abnormalities
- Birthmarks

Treatment

- Topical steroids are useful for limited affected areas.
- Recognition helps parents limit unintentional scratching and trauma of the lesions.
- In children, more generalized disease is treated with antihistamines and oral cromolyn.
- Systemic disease is managed in a stepwise manner:
  - Antihistamine H_1 blockers are used for flushing and pruritus.
  - Antihistamine H_2 blockers or proton-pump inhibitors are used for gastrointestinal manifestations.
  - Oral cromolyn sodium can be helpful for diarrhea and abdominal pain.
  - Nonsteroidal anti-inflammatory agents can be used for severe flushing; they act by blocking mast cell release of prostaglandin D_2.
- Photochemotherapy with psoralen plus ultraviolet A can be useful in extensive cases.
- Treatment includes avoidance of mast cell stimulators, such as morphine, codeine, dextromethorphan.

Pearls

- Stroking a lesion of urticaria pigmentosa produces a wheal surrounded by intense erythema—Darier's sign—and is the hallmark of urticaria pigmentosa.

Fig. 3.20 Mastocytosis. A single small brown macule was stroked with the wood end of a cotton-tipped applicator. Intense erythema occurred in about 1 minute. This was rapidly followed by intense swelling and itching.

Fig. 3.21 Mastocytosis. A few too many slightly elevated plaques, colored red to brown, typically occur between birth and 2 years of age. The trunk is the most common site.

Pediatric Considerations

- Most cases of urticaria pigmentosa occur in the neonate and infant. Parents need reassurance that this is not a life-threatening problem, and it often resolves later in life.
- Multiple, red-brown, slightly elevated macules and patches typically occur between birth and 2 years of age. The trunk is the most common site.
- Parents must know about potential mast cell degranulators or triggers and avoid them whenever possible. Nonimmunologic mast cell degranulators are shown in Box 3.1. Children with urticaria pigmentosa may be at increased risk for anaphylaxis after insect stings. The parents should carry an epinephrine (adrenaline) pen (EpiPen Jr.) and should ensure that their children wear a medical alert bracelet.

Box 3.1 Nonimmunologic Mast Cell Degranulators

Venoms (snakes, insect stings)
Aspirin and other nonsteroidal anti-inflammatory drugs
Iodine-containing radiocontrast media
Narcotics (codeine, morphine)
Polymyxin B
Dextran
Jellyfish stings
Neuromuscular blocking agents (used in general anesthesia)
Sympathomimetics (amphetamines, ephedrine, dextromethorphan)

Fig. 3.22 Urticaria pigmentosa. Lesions vary in size and number. Many patients present with just a few brown macules that may be misinterpreted as café-au-lait spots. Other patients have many large lesions. These patients are unstable and may have many episodes of severe itching.

Fig. 3.23 Urticaria pigmentosa. Lesions tend to be larger in children than adults. Lesions in children are more hyperpigmented than erythematous. The trunk is the most commonly affected area. Involvement of the face and scalp does occur. Vesicles and blisters may form on lesions in children. These blisters are tense and may become hemorrhagic, but they heal without scarring. The tendency to form blisters resolves after age 3 years.

Pruritic Urticarial Papules and Plaques of Pregnancy

Description

- Pruritic urticarial papules and plaques of pregnancy (PUPPP) are the most common gestational dermatosis.
- PUPPP is characterized by intensely pruritic papules and urticarial plaques that start on the abdomen in striae, late in the third trimester.
- PUPPP is not life-threatening, but it does cause discomfort and must not be confused with herpes gestationis.

History

- The average age of onset is 25 years.
- The incidence is 1 in 160 pregnancies.
- About 40% of cases involve primigravidas, 30% involve women who are pregnant for the second time, and about 15% involve women who are pregnant for the third time.
- Most cases begin late in the third trimester near delivery, but they can occur in the first or second trimester and rarely in the immediate postpartum period.
- The mean duration of involvement is 6 weeks, but the rash is usually not severe for more than 1 to 3 weeks.
- Recurrence with future pregnancies is unusual but possible.

Skin Findings

- The problem begins on the abdomen, within striae of the abdomen in 90% of patients.
- After a few days, the hive-like rash spreads symmetrically and may involve the hips, buttocks, upper and lower extremities, chest, and back.
- The hands, feet, palms, soles, and face are usually not involved.
- Itching is moderate to intense but occasionally can be debilitating.
- Lesions begin as red papules, linear patches, or plaques that are often surrounded by a pale halo.
- They quickly increase in number and may become confluent, forming larger edematous urticarial plaques. Excoriations occur uncommonly, and blisters do not occur.

Laboratory and Testing

- Biopsy reveals a slight to moderate perivascular infiltrate of mononuclear cells, some eosinophils, and variable epidermal spongiosis, usually consistent with other hive-like processes.
- There are no laboratory abnormalities.
- The results of direct immunofluorescence of lesional and perilesional skin are negative.
- A lack of immunofluorescence separates the disease from herpes gestationis, which would show positive direct immunofluorescence with immunoglobulin G and C3 at the basement membrane zone.

Course and Prognosis

- There are no associated complications during pregnancy and delivery.
- Recurrences in subsequent pregnancies are unusual but possible.
- The delivered infants do not develop the eruption.
- If vesicles and bullae develop, direct immunofluorescence should be performed to evaluate for herpes gestationis.

Discussion

- Congenital abnormalities are absent or are unrelated to this disease.
- Unlike acute urticaria, the eruption remains fixed and increases in intensity, clearing in

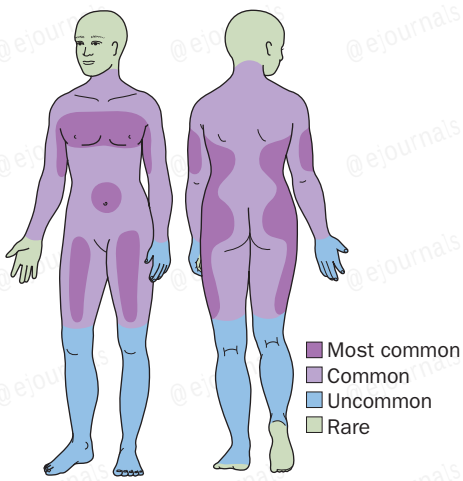

Fig. 3.24 Pruritic urticarial papules and plaques of pregnancy distribution diagram.

some cases before or within 1 week of delivery.
- Because the eruption occurs in a state of pregnancy, consultation with the obstetrician is usually advised.

Treatment

- Treatment is typically supportive.
- The expectant mother can be assured that the pruritus will quickly terminate before or after delivery.
- Itching can be relieved with medium to super potency topical steroids, with cool wet dressings, antipruritic lotions, and antihistamines.
- Prednisone 30 to 40 mg per day may be required if the pruritus becomes intolerable, but this is rarely needed.

Fig. 3.25 Pruritic urticarial papules and plaques of pregnancy. Lesions begin as red papules surrounded by a narrow, pale halo. They increase in number and become more confluent. Unlike urticaria, these lesions remain fixed and may not disappear until after delivery.

Fig. 3.26 Pruritic urticarial papules and plaques of pregnancy. The abdomen is often the initial site of involvement. Initial lesions may be confined to striae.

Fig. 3.27 Pruritic urticarial papules and plaques of pregnancy. Lesions spread in a symmetric fashion to involve the buttocks, legs, arms, and back of the hands. The face is not involved.

Fig. 3.28 pruritic urticarial papules and plaques of pregnancy. Diffuse, generalized pink hive-like macules coalescing into larger macules, over the entire trunk, which originated in the abdominal striae of this pregnant woman. No vesicles or blisters are present.

Fig. 3.29 Pruritic urticarial papules and plaques of pregnancy. Sometimes lesions are predominately papular without the presence of abdominal striae.

Acne, Rosacea, and Related Disorders

4

James G. H. Dinulos

Acne

Description

- Acne is a papular or pustular eruption involving the face, chest, and back.

History

- Acne may occur at any age but is more common in the teenage years and may persist well into adulthood.
- Twenty percent of affected individuals develop severe acne resulting in scarring.
- Acne can run in families, and those with a family history of acne often develop acne at an earlier age.
- If both parents have acne, there is a 75% chance that a given child will develop acne.
- Plugged follicles, increased sebum production, *Propionibacterium acnes,* and inflammation are thought to promote acne.
- The role of diet in the pathogenesis of acne remains unclear, although consumption of dairy products and simple sugars has been implicated in some studies.
- There are several variants of acne:
  - Steroid acne (papular and pustular acne on the face and torso 2 to 5 weeks after a steroid has been taken)
  - Neonatal acne (younger than 1 month of age)
  - Infantile acne (1 month to 1 year of age)
  - Acne necrotica (scarring scalp acne)
  - Acne excoriée (acne that has been manipulated by the patient, leaving erosions and scars)
  - Acne conglobata (severe cystic scarring acne on chest, back, and shoulders)
- Consider a hyperandrogen state, such as congenital adrenal hyperplasia or polycystic ovarian syndrome.

Skin Findings

- Acne lesions are divided into noninflammatory and inflammatory lesions.
- Noninflammatory lesions consist of open comedones (blackheads) and closed comedones (whiteheads).
- Inflammatory lesions consist of red papules, pustules, nodules, and cysts.
- Recurring rupture and re-epithelialization of cysts lead to epithelium-lined sinus tracks, often accompanied by disfiguring scars.
- Eroded papules are seen in patients who pick acne papules (acne excoriée).

Nonskin Findings

- Patients with androgen excess can develop signs of virilism (thinning of scalp hair, hirsutism) and precocious puberty.
- Rarely, acne occurs in association with fever, bone, and joint problems (acne fulminans).
- Significant psychosocial issues may be present, including depression, anxiety, and social withdrawal.

Laboratory and Biopsy

- Laboratory evaluation is indicated for female patients with persistent acne and evidence of

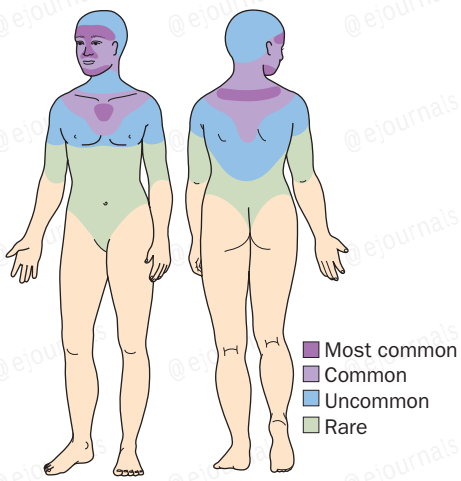

Fig. 4.1 Acne distribution diagram.

a hyperandrogenic state (facial hair, muscle hypertrophy, irregular menses).
- Tests include measurements for testosterone, follicle-stimulating hormone, luteinizing hormone, and dehydroepiandrosterone sulfate.
- Bacterial and fungal cultures can be done to rule out infectious folliculitis.

Differential Diagnosis

- Rosacea (flushing and blushing but no comedones)
- Bacterial (gram-negative folliculitis) and yeast folliculitis (not typical on the face)
- Keratosis pilaris (location more typical on the extensor upper arms)
- Perioral dermatitis (comedones are not seen)

Course and Prognosis

- Men have more severe disease than women; men are less likely to seek early medical treatment.
- Androgens can aggravate acne. It is important to ask about use of anabolic steroids, especially in athletes.
- Acne flares may be seen during periods of stress, before menstrual periods, with certain medications (corticosteroids, lithium, anticonvulsants, antituberculosis medications, and iodides).
- The propensity to form scars varies from patient to patient.
- The redness and pigmentation after resolution of acne lesions may take many months to fade.
- Patients often confuse red macules for scars (pseudoscars).
- Areas where the skin is rubbed, such as under a hat or under a chin strap, may have accentuated acne (acne mechanica).
- Acne occurs with variable severity. Sometimes only comedones appear; at other times cystic lesions predominate.
- Acne usually begins between ages 10 years and 15 years and lasts for 5 to 10 years.
- Children who require oral medications at an early age tend to have a more severe course.
- Adult women can have chronic low-grade acne that can be challenging to manage.
- Girls who develop a large number of acne lesions (noninflammatory and/or inflammatory) at an early age are likely to develop more severe acne.

Treatment

- Therapy should account for medical, financial, and psychosocial factors.
- When possible, regimens should be simplified, using the fewest possible medications.
- Decrease the risk for antibiotic resistance by limiting oral antibiotic therapy to 3 months and combining oral and topical antibiotics with benzoyl peroxide.
- It takes at least 2 months for most topical medications to show their full effect, so patience must be exercised.
- Most treatment is continual and prolonged because it is control—not cure—that is most often achieved.
- A patient's propensity to scar should be determined. Patients who show evidence of scarring should be treated systemically and followed closely.
- Isotretinoin should be considered if acne does not improve after 3 months of oral antibiotics. Patients with nodulocystic acne may be started on isotretinoin as initial therapy.
- When managing acne, skin sensitivity and the presence of noninflammatory and inflammatory lesions should be considered.

Skin Sensitivity

- The skin should be gently cleansed with a mild soap and tepid water.
- Patients should be encouraged not to excessively scrub the skin.
- Deep cleaning brushes are best used separately from drying exfoliating agents (e.g., salicylic acid, benzoyl peroxide, and retinoids).
- Let the skin dry before applying topical agents.
- Medications should be applied in a thin layer with a gentle message to acne-prone sites.
- Patient should not apply medications to normal skin where acne lesions do not occur.
- If the skin becomes red or dry, one should ensure that excessive medication is not being

applied and the correct vehicle was chosen for the patient's skin type.
- Solutions and gels are better for oily skin, whereas creams and lotions are better for dry skin.
- Lower concentration medications are better for patients with sensitive skin.
- Hair conditioners and oils should be avoided.
- If cosmetics are used, they should be oil free and water based.
- Patients should not pick or pop their acne lesions.
- To avoid redness and dryness, retinoids should be applied 30 minutes after skin cleansing.

Noninflamed Blocked Pores (Comedones—Blackheads and Whiteheads)
- Agents that gently exfoliate the top layer of skin and have antibacterial properties (e.g., benzoyl peroxide) are used in combination with agents that correct follicular plugging (e.g., tretinoin, adapalene, tazarotene). One agent is usually applied in the morning and the other in the evening.
- Prescription and over-the-counter products used for exfoliation contain sulfur, salicylic acid, resorcinol, and benzoyl peroxide.
- There are many over-the-counter benzoyl peroxide gels, lotions, and creams, ranging in strength from 2.5% to 10%.
- Retinoid medications (tretinoin, adapelene, and tazarotene) primarily affect follicular plugging and produce mild anti-inflammatory effects.
- Patients should apply retinoids at night.

Fig. 4.2 Acne. Multiple open comedones in the ear of a patient with noninflammatory acne. The ear is a common site to see open comedones and can be removed with a comedone extractor and gentle pressure.

- The following are the most commonly used retinoid preparations:
  - **Tretinoin**

Retin-A gel (0.025%, 0.01%)
Tretinoin cream (0.1%, 0.05%, 0.025%)
Retin-A micro (0.04, 0.08, 0.1%)
Avita cream and gel (0.025%)
Renova cream (0.02%)
Atralin gel (0.05%)
Tretin-X cream (0.025%, 0.0375%, 0.05%, 0.075%, 0.1%)
Veltin, Ziana (tretinoin 0.025% combined with clindamycin 1.2%)

  - **Adapalene**

Adapalene (Differin) 0.1% gel, cream, lotion, and 0.3% gel
Epiduo gel (adapalene–benzoyl peroxide 0.1%–2.5%)
Epiduo Forte (adapalene–benzoyl peroxide 0.3%–2.5%)

- **Tazarotene**

Tazorac 0.05%, 0.1% gel and 0.5%, 0.1% cream
Fabior 0.1% foam

- Adapalene, Renova, and Atralin cause less dryness and redness.
- Adapalene is the least photosensitizing retinoid.
- Tazarotene effectively removes comedones but can be very irritating. Applying the cream formulation or having the patient use the gel formulation and wash it off at increasing intervals (short contact therapy) may lessen irritation.
- Tazarotene has a Pregnancy Category X warning.
- Azaleic acid (Azelex) relieves follicular plugging and has antimicrobial activity.
- Facial peels (glycolic acid, salicylic acid) effectively open plugged pores and should be considered for most patients.

Inflamed Pores (Papules and Pustules)
- Inflammatory acne is treated with antimicrobial agents in combination with retinoids and benzoyl peroxide.
- Topical antimicrobial preparations include benzoyl peroxide, benzoyl peroxide antibiotic combinations (e.g., BenzaClin, Duac, Acanya, Onexton), and sulfur preparations (e.g., Klaron, Aczone).

- Sulfacetamide and sulfur washes (e.g., AVAR, Plexion, Rosanil, Clenia) are effective and convenient.
- Oral antibiotics should be started at higher doses and quickly tapered to minimize side effects.
- Typical starting dosages are doxycycline 100 mg twice a day and minocycline 100 mg twice a day.
- Maximal effect of an oral antibiotic is achieved after 2 months.
- Oral antibiotics, with the exception of rifampin, are not thought to lower the contraceptive efficacy of oral contraceptives.
- Photodynamic therapy and lasers have been used to treat inflammatory acne, but their use is limited by pain and expense.

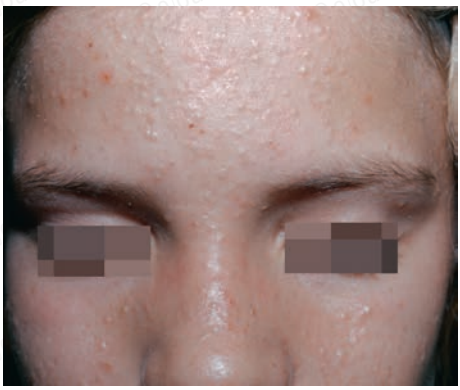

Fig. 4.3 Acne. Multiple closed comedones on the forehead. Moderate to severe acne responds slowly to treatment. Tazarotene may be used in combination with manual extraction.

Fig. 4.5 Acne vulgaris. Papules and pustules seen in moderate inflammatory acne vulgaris.

Fig. 4.4 Mild inflammatory acne. Mild acne with papules, pustules, and comedones.

Fig. 4.6 Acne. Multiple pustules and cysts in exuberant inflammatory acne.

Fig. 4.7 Acne vulgaris. Multiple pustules and cysts in inflammatory acne vulgaris.

Inflamed Nodules and Cysts (Nodulocystic Acne)

- Acne not responsive to intensive therapy with oral antibiotics and topical retinoids requires alternative therapy.
- A small amount of triamcinolone (2.5 mg/mL) can be injected into individual cysts, but there is a risk for cutaneous atrophy.
- Short courses of systemic corticosteroids improve acne, but acne has a tendency to flare after treatment. Prednisone 20 mg twice a day for 1 week can rapidly control severely inflamed cystic acne.
- Oral contraceptives (e.g., Ortho Tri-Cyclen, Yaz, Estrostep, Beyaz) are beneficial for female patients with acne who desire contraception.
- Spironolactone at doses of 25 to 100 mg twice daily improves acne in many women, especially adult women. Spironolactone may be taken with oral contraceptives, and pregnancy should be avoided.
- Isotretinoin is the most consistent and effective treatment for acne. A clinical cure can be achieved in approximately 80% of patients with a cumulative dose of 120 to 150 mg/kg over 4 to 5 months.

Changes in Pigment and Scarring

- For scarring, referral to a dermatologic surgeon is advisable only after the acne is quiescent for at least 1 year. This allows for maximal normal healing before any invasive procedure.
- Red macules fade with time and are not true scars.
- Some patients, especially if they have a dark complexion, develop light and/or dark macules that take many months or years to resolve and that are permanent in some patients.
- Scars may be raised and thick (hypertrophic and keloid) or depressed (pitted or broad-based).
- Treatments for pigment changes include hydroquinone, tretinoin, azelaic acid, chemical peeling, and laser resurfacing.
- Treatment for acne scars includes excision, laser, dermabrasion, chemical peeling, injection with “fillers” (hyaluronic acid, collagen, others), and microneedling.
- Intralesional corticosteroid (Kenalog 2.5–10 mg/mL) injections and application of silicone gel sheeting can be helpful for thick scars.
- Alternative therapies (e.g. tree tree oil, oral supplements, maunka honey, tannis, fruit acids, brewers yeast) may be utilized by patients. Be sure to ask patients about their use, since they may be counter-productive with traditional therapies.

When to Refer

- Patients with the possibility of an underlying endocrine abnormality should be evaluated in consultation with a dermatologist and an endocrinologist.

- Patients with scarring acne or with acne that fails to respond to conventional treatment should be referred to a dermatologist.

Pearls

- Combination therapy is essential to successful management of acne.
- Set realistic expectations with patients on the first visit, but be encouraging, and let patients know that acne therapy is extremely effective when used consistently and appropriately.

Pediatric Considerations

- Neonates and infants can develop acne. Topical medicine is usually sufficient to control the acne; however, if recalcitrant inflammatory lesions or scarring is present, oral erythromycin or isotretinoin may be required.
- Tetracycline, doxycycline, and minocycline should not be used in children younger than 12 years to avoid staining permanent teeth.

Fig. 4.8 Severe comedonal, inflammatory, and cystic acne on the chest.

Fig. 4.9 Moderate comedonal and inflammatory infantile acne. Selectively treat acne prone sites to avoid irritation on normal skin.

Fig. 4.10 Keratosis pilaris. Fine papules on an erythematous base are characteristic of keratosis pilaris that resembles acne.

Fig. 4.11 Acne vulgaris. Moderate inflammatory and cystic acne vulgaris.

Fig. 4.12 Acne vulgaris. Moderate inflammatory and cystic acne vulgaris.

Fig. 4.13 Acne vulgaris typically starts on the central forehead, nose, and chin (T distribution).

Fig. 4.14 Acne vulgaris. Severe inflammatory and cystic acne vulgaris on the forehead.

Fig. 4.15 Severe inflammatory acne vulgaris may be associated with fever and joint pain.

Fig. 4.16 Acne excoriée is produced from picking acne lesions and may result in delayed healing and scarring.

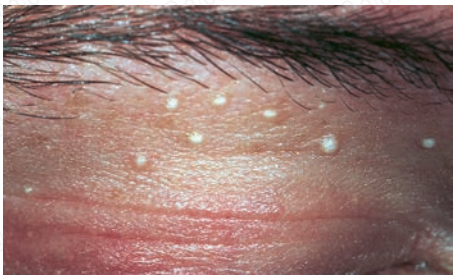

Fig. 4.17 Milia on the eyelid may appear similar to a closed comedone.

Perioral Dermatitis

Description

- Perioral dermatitis is a distinctive scaly papular eruption around the mouth, nose, and eyes that occurs almost exclusively in women but can also occur in children.

History

- The eruption may start around the mouth but may also involve the perinasal and periocular regions (periorificial dermatitis).
- Usually this condition is asymptomatic, but some adult patients describe burning.
- The cause is unknown.
- Medications (topical, inhaled, systemic corticosteroids), cosmetic products, moisturizers, physical factors (ultraviolet light, heat, cold), microorganisms (*Fusobacterium* and *Candida* species, *Demodex folliculorum*), and oral contraceptives are suspected triggers.

Skin Findings

- Pinpoint papules and pustules on a red scaly base occur on the chin, in the nasolabial folds, and around the eyes.
- There is a clear zone around the vermilion border.
- Pustules on the cheeks adjacent to the nostrils are common.

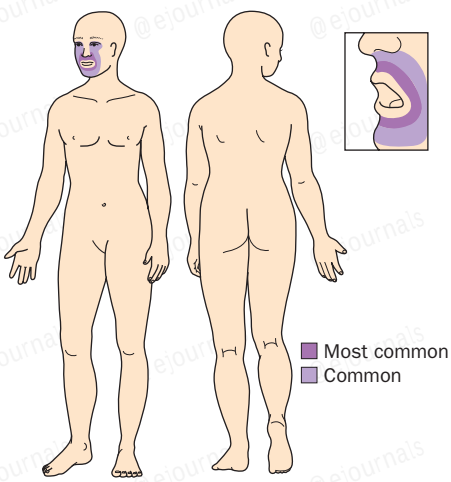

Fig. 4.18 Perioral dermatitis distribution diagram.

Differential Diagnosis

- Acne
- Rosacea
- Seborrheic dermatitis
- Atopic (eczematous) dermatitis
- Impetigo
- *Demodex* folliculitis

Course and Prognosis

- There are varying degrees of involvement.
- The disorder lasts 2 weeks to 4 years with spontaneous resolution.
- Oral antibiotics clear most patients within 4 weeks.
- Relapse is common.
- Patients are retreated with renewed activity, and sometimes long-term maintenance is required.

Treatment

- Topical treatment involves once- or twice-daily use of metronidazole cream or gel (0.75% or 1%), sodium sulfacetamide 10% plus sulfur 5% (Sulfacet-R), sodium sulfacetamide (Klaron), clindamycin lotion, pimecrolimus cream 1% (Elidel), tacrolimus 0.03%, 0.1% ointment (Protopic), and azelaic acid (Finacea).
- Oral antibiotic treatment includes tetracycline (500 mg twice a day), erythromycin (500 mg twice a day), doxycycline (100 mg twice a day), or minocycline (100 mg twice a day). Oral antibiotics are prescribed for 2 to 4 weeks, and many patients respond to lower doses.
- After it is controlled, most patients require daily application of metronidazole or a sulfur-based medication.

Fig. 4.19 Perioral dermatitis in an infant inappropriately treated with topical steroids.

Pearls

- Patients should minimize use of antiaging creams and moisturizers with additives.
- A fragrance-free moisturizer can be helpful to control dryness.
- Discontinuing topical steroids will cause the disease to flare, but this is necessary to cure the disease.

Fig. 4.20 Perioral dermatitis. Group V topical steroids were used for months. The eruption flared each time they were discontinued.

Fig. 4.22 Perioral dermatitis. Pinpoint pustules next to the nostrils may be the first sign or only manifestation of the disease.

Fig. 4.21 Perioral dermatitis: a classical case with the typical distribution. Pinpoint papules and pustules with sparing around the mouth.

Fig. 4.23 Perioral dermatitis. Pinpoint papules and pustules similar to those seen next to the nostrils are commonly seen at the lateral canthus.

Rosacea (Acne Rosacea)

Description

- Rosacea is a common facial eruption characterized by redness, telangiectasia, flushing, blushing (vascular component), and papules and pustules (inflammatory component).

History

- Patients are usually older than 30 years.
- Rosacea can occur in children.
- The cause is unknown but involves genetic factors (more common in people of Celtic or Northern European descent), ultraviolet light exposure, microorganisms (*Demodex* species, *Staphylococcus epidermidis, Bacillus oleronius*), skin sensitivity, and food triggers (alcohol, spicy foods).
- Innate immunity is activated, especially antimicrobial peptides.

Skin Findings

- Papules and pustules occur on the forehead, cheeks, and nose and around the eyes.
- Erythema and/or telangiectasias are present.
- Severe cases have numerous pustules, telangiectasia, diffuse erythema, oily skin, and edema (cheeks and nose).
- Chronic, deep inflammation of the nose leads to an irreversible skin thickening called *rhinophyma*. This is more common in men.
- Uncommonly, rosacea papules can involve the scalp, the torso, and the arms and legs.

Nonskin Findings

- Ocular symptoms include mild conjunctivitis with soreness, grittiness, and lacrimation.
- Ocular signs include conjunctival hyperemia, telangiectasia of the lid, blepharitis, superficial punctate keratopathy, chalazion, corneal vascularization and infiltrate, and corneal vascularization and thinning.

Laboratory and Biopsy

- The diagnosis usually is made with clinical examination. Tests are unnecessary.
- If lesions are atypical, bacterial culture is obtained to rule out folliculitis.
- If there is scaling, a potassium hydroxide test is performed to rule out tinea.
- A biopsy can be considered to rule out lupus or granulomatous disease (sarcoidosis).

Differential Diagnosis

- Acne (no comedones in rosacea)
- Pustular tinea
- Perioral dermatitis
- Infectious folliculitis (staphylococcal, gram-negative acne)
- Lupus erythematosus
- Sarcoidosis

Course and Prognosis

- Rosacea is exacerbated by ingestion of hot foods and drinks, ingestion of alcohol (red wine), heat, sunlight, and topical medications that irritate the skin, such as antiwrinkle creams and chemical peels that exfoliate the skin.
- The condition is chronic (years) with episodes of activity followed by quiescence.
- It may result in permanent swelling of the periocular tissues and firm facial edema.

Treatment

- The patient should avoid known factors that exacerbate rosacea, such as hot food and drinks, spicy foods, red wine, and sunlight.
- Green-based cosmetic foundations will mask the redness.

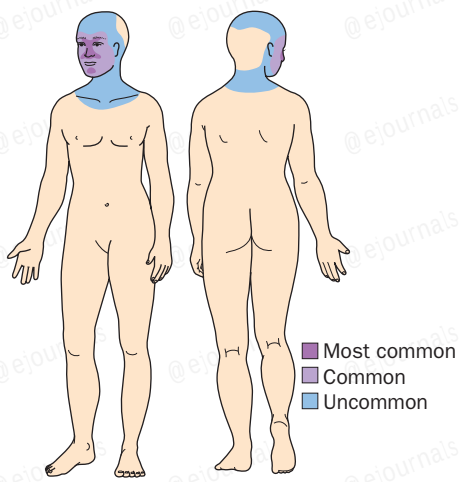

Fig. 4.24 Rosacea distribution diagram.

Fig. 4.25 Severe rosacea showing redness, papules, pustules, rhinophyma, and conjunctivitis. Oral antibiotics and topical ivermectin provided control over 3 months.

Fig. 4.27 Rhinophyma. Untreated inflammation on the nose results in irreversible hypertrophy that may be treated with surgery.

Fig. 4.26 Rosacea. Deep erythema of the nose is highly characteristic of rosacea. Long-term treatment with oral antibiotics is often required. Drying topical therapy with sulfacetamide and sulfur is effective.

Fig. 4.28 Papulopustular rosacea. Papules and pustules and the absence of comedones strongly favor the diagnosis of rosacea rather than acne.

Fig. 4.29 Rosacea erythema and telangiectasia may be the only sign of rosacea. The diagnosis may be difficult to establish because these same changes appear in some light-complexion people. These changes may be treated with laser. Brimonidine and oxymetazoline improve redness but are associated with rebound redness in many patients.

- Sunscreens are recommended.
- The pustular component is treated topically or systemically.
- For topical treatment, ivermectin (Soolantra), metronidazole (MetroGel, MetroCream, MetroLotion, and Noritate), and sulfacetamide plus sulfur lotion (Avar, Plexion TS, and Rosac) are the most effective. Avar is available as a cream or gel. A special green formulation of Avar cream and gel masks red skin. Topical clindamycin and erythromycin are less effective. Azelaic acid 15% gel (Finacea) is effective but can be drying. Brimonidine 0.5% (Mirvaso) and Oxymetazoline 1% (Rhofade) decrease facial redness but frequently are irritating.
- Systemic therapy is more effective. Doxycycline 100 mg twice a day or minocycline 100 mg twice a day in a 2- to 4-week course usually controls the pustules. In many patients, this condition then responds to lower doses.
- Oracea is a once-daily, 40 mg, controlled-release oral doxycycline. The dose falls below doxycycline's threshold of antibiotic activity. It is the only oral medication approved by the U.S. Food and Drug Administration (FDA) for treating inflammatory rosacea.
- Ocular symptoms are treated with systemic antibiotics.
- Oral medication is stopped or tapered after the condition resolves.
- Recurring disease is retreated; then oral medication is tapered to the minimal dosage that provides adequate control.
- For chronic relapsing cases or failure to respond, isotretinoin 0.5 mg/kg/day for 20 weeks should be considered.
- Rhinophyma is treated with electrosurgery, carbon dioxide laser surgery, and plastic surgery.
- Rosacea has been successfully treated with photodynamic therapy.

Pearls

- Rarely, rosacea can present with granulomatous lesions (granulomatous rosacea) and mimic lupus or sarcoidosis.
- Rosacea patients should wash with mild facial cleansers and avoid antiaging creams.
- Rosacea may worsen for 1 to 2 weeks before improving with topical medications.

Fig. 4.30 Rosacea papules and pustules on the nose are treated initially with oral antibiotics. Topical treatment should start at the same time as treatment with ivermectin, sulfacetamide and sulfur, or metronidazole.

Fig. 4.31 Steroid rosacea occurs when a patient discontinues long-term topical steroid therapy. There is a rapid and intense flare with papules and pustules. Application of the offending medication is resumed and reestablishes the vicious cycle.

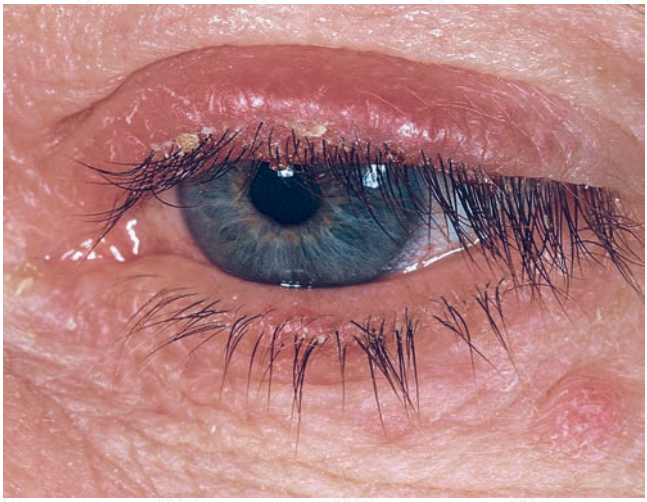

Fig. 4.32 Ocular complications often occur in patients with rosacea. The diagnosis should be considered when a patient's eyes have one or more of the following signs and symptoms: watery or bloodshot appearance, foreign body sensation, burning or stinging, dryness, itching, light sensitivity, blurred vision, telangiectasias of the conjunctiva and lid margin, or lid and periocular erythema. Blepharitis, conjunctivitis, and irregularity of the eyelid margins also may occur.

Hidradenitis Suppurativa

Description

- Hidradenitis suppurativa (HS) is a chronic recurring disorder of the follicular unit, producing extremely painful, deep-seated nodules, cysts, sinus tracts, and scars in the apocrine gland–bearing areas of the body, including the axillae and the inguinal and anogenital regions.

History

- HS is a rare disorder and is more common in females.
- The mean age of onset is the early 20s.
- It presents with painful recurrent "boils" that rupture, forming sinus tracts and scars.
- Axillary and inguinal involvement is more common in females, whereas perianal and buttock involvement is more common in males.
- The most common site of involvement is the axillae.
- It usually does not appear until after puberty, although prepubertal children are sometimes affected. Most cases appear in the second and third decades of life.
- It may be clustered in families and inherited in an autosomal dominant manner.
- The precise etiology of HS is not known, but it likely involves follicular occlusion from infundibular hyperkeratosis and follicular epithelium hyperplasia. Perifollicular inflammation and follicular rupture, result in cysts, abscesses, and sinus tracts.
- Secondary infection and inflammation are common.
- HS may be associated with Crohn's disease and rheumatologic conditions (e.g., spondyloarthropathies).

Skin Findings

- The hallmark is the double comedone (a blackhead with two or more surface openings "tombstones").
- Pink to red nodules are rounded without central necrosis, lasting up to 2 weeks. Extensive, deep, dermal inflammation results in large, painful, draining malodorous abscesses.
- Sinus tracts form, resulting in firm, rope-like scars.
- Follicular papules, pustules, and epidermal cysts may be associated with classical HS skin lesions.

Laboratory

- Biopsy shows follicular occlusion by keratinous material, folliculitis, and secondary destruction of the skin adnexa (apocrine glands) and subcutis.

Differential Diagnosis

- Acne
- Furuncle or carbuncle
- Infected Bartholin's gland
- Inflamed epidermal cyst
- Pilonidal cyst
- Lymphogranuloma venereum
- Scrofuloderma
- Actinomycosis
- Developmental fistulae
- Crohn's disease

Course and Prognosis

- HS is active for approximately 20 years.
- Patients may experience premenstrual flares.

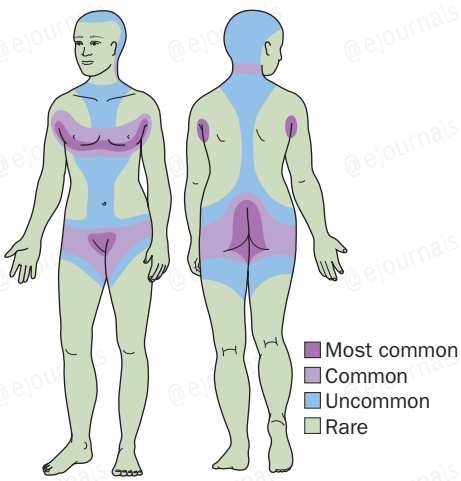

Fig. 4.33 Hidradenitis suppurativa distribution diagram.

- Factors exacerbating HS include obesity, smoking, heat, exercise, sweat, tight-fitting clothing, deodorant, shaving, and menstruation.
- Complete remission is usual after menopause.
- Pregnancy and breast-feeding may induce remission.
- Patients with chronic ulcerations are at risk for squamous cell carcinoma.
- Perianal disease portends a worse prognosis.
- Even patients with few lesions may exhibit a chronic relentless course that negatively affects their quality of life.

Treatment

- Large fluctuant cysts are incised and drained.
- Intralesional triamcinolone acetonide (Kenalog) 5 to 10 mg/mL is administered for smaller cysts.
- Weight loss, smoking cessation, and loose clothing can sometimes be helpful to improve symptoms.
- Long-term oral antibiotics are a mainstay of treatment. Agents include doxycycline 100 mg twice a day and minocycline 100 mg twice a day. Lower dosages are tried for maintenance.
- Second-line antibiotics include trimethoprim–sulfamethoxazole Bactrim DS (one by mouth twice a day), metronidazole 375 mg twice a day, and clindamycin 150 mg twice a day. The combination of clindamycin 300 mg twice daily and rifampin 500 daily for 10 weeks has been effective.
- Oral contraceptives are sometimes helpful, especially with premenstrual flares.
- Isotretinoin 1 mg/kg/day for 20 weeks is effective in selected cases (best in early nonscarred sinus tract lesions).
- Cytokine blocking agents, such as anakinra (IL-1), ustekinumab (IL-12/23), infliximab (TNF-α), etanercept (TNF-α), and adalimumab (TNF-α), are effective in selected cases.
- Adalimumab (Humira) is approved by the FDA for the treatment of HS.
- Dapsone, zinc gluconate, antiandrogens, and cyclosporine have been administered with success in select patients.
- Surgical excision is often the only solution.
- Local opening of the sinus tract with unroofing is frequently helpful to decrease pain and sinus tract advancement.
- Laser hair removal may be of benefit.
- Cyst and sinus tract ablation with CO_2 and Nd:YAG laser may be helpful.
- Powder (e.g., Zeasorb) and topical antiperspirants (e.g., Xerac) reduce friction.
- Chlorhexidine gluconate 4% solution, 10% benzoyl peroxide, and bleach baths decrease bacterial colonization.
- Lidocaine 5% ointment, diclofenac 1% gel, ice packs, and nonsteroidal anti-inflammatory drugs are helpful for pain management.

Pearls

- Rarely HS occurs in prepubertal children—even those who are not obese.
- Early disease can present with very small tender pustules in the groin and axillae.
- Suspect hidradenitis when women complain of "boils in the groin."
- Refer patients for depression and pain to appropriate specialists.

Fig. 4.34 Hidradenitis should be suspected when a patient complains of boils in the groin. Comedones, which are markers for this disease, should be carefully sought.

Fig. 4.35 Hidradenitis. Double and triple comedones are blackheads with two or more surface openings that communicate under the skin. They are a hallmark of hidradenitis. The axillae, the area under the breast, the groin, and the buttock area should be examined for markers of the disease.

Fig. 4.37 Hidradenitis may occur under the breasts. This is a particularly severe case with confluent cysts.

Fig. 4.36 Hidradenitis of the axillae. Cysts were present for months and were eventually controlled with long-term oral antibiotics.

Fig. 4.38 Hidradenitis. Cysts and sinus tracts are hallmarks of hidradenitis suppurativa and are extremely painful.

Fig. 4.39 Sinus tracts may be unroofed to remove gelatinous material and prevent further spread to the sinus tract.

Fig. 4.40 Hidradenitis suppurativa. The inframammary fold is a common location for hidradenitis suppurativa.

Fig. 4.41 Painful cysts of hidradenitis suppurativa should be treated with incision and drainage.

Hyperhidrosis

Definition

- The term *hyperhidrosis* is used to describe excessive sweat production.
- Hyperhidrosis is common and can involve localized or widespread areas of skin.

History

- Hyperhidrosis can be classified according to anatomic location (axillary, palmar, plantar), underlying stimulus (emotional, thermal, drug, toxin), or neural origin (cortical, hypothalamic, medullary, spinal, axonal).
- Sweating at night can be caused by a number of underlying systemic conditions (e.g., Hodgkin's lymphoma).
- Primary hyperhidrosis (not due to underlying medical condition or medication) occurs in 3% of the population, stops with sleep, and is bilateral and symmetric.
- Exercise and emotional stress are the most common causes of hyperhidrosis.
- Careful history is important to determine the underlying cause of hyperhidrosis.

Skin Findings

- Chronic effects of excessive skin moisture include dry, flaky skin with cracks and fissures.
- Patients with excessively moist skin are susceptible to bacterial overgrowth (pitted keratolysis) and yeast infection.
- Patients with pitted keratolysis develop small superficial pits on the soles, associated with intense foot odor.

Nonskin Findings

- Nonskin findings are dependent on the underlying cause of hyperhidrosis.

Laboratory and Biopsy

- Sweat turns black when combined with iodine and starch (starch–iodine reaction). The three methods described here use the starch–iodine reaction to semiquantify sweat production:
  - Iodinated starch powder (0.5–1 g of iodine crystals to 500 g of soluble starch, stored in an airtight bottle) applied directly to the skin
  - Iodine solution applied to the skin and dried followed by a light dusting of starch powder
  - Iodine-impregnated paper (made by exposing 100 sheets of iodine paper to 1 g iodine crystals for 1 week in an airtight container) exposed to a sweaty skin surface (paper–iodine technique)
- Laboratory evaluation for underlying medical conditions should be directed by history and physical examination.

Differential Diagnosis

- The following conditions may induce hyperhidrosis:
  - Infections (febrile illnesses, tuberculosis)
  - Metabolic or endocrine (hyperthyroidism, diabetes mellitus, obesity, carcinoid syndrome)
  - Vasomotor (Reynaud's phenomenon)
  - Neurologic (Parkinson's disease, postencephalitis)
  - Neoplasia (lymphoma)
- Many drugs can induce hyperhidrosis as a side effect (insulin, caffeine)
- Toxins, such as mercury and arsenic, can produce hyperhidrosis

Course and Prognosis

- Hyperhidrosis is socially and occupationally debilitating for patients.
- Treatment of underlying systemic conditions improves hyperhidrosis.

Treatment

- Topical application of 6% (Xerac) or 20% (Drysol) aluminum chloride hexahydrate with or without plastic wrap occlusion, at night for 3 to 4 nights, and then as needed is helpful for most patients. Mild skin irritation is a common side effect.
- Topical 0.5% to 2% glycopyrrolate is effective but may cause anticholinergic side effects if used over broad areas.
- Tap-water iontophoresis performed daily for 15 to 30 minutes and then two or three times a week can be an effective method to control palmoplantar hyperhidrosis.
- Oral glycopyrrolate and oxybutynin can diminish sweating in some patients but can cause anticholinergic side effects.

- Botulinum toxin inhibits release of acetylcholine and is a very effective method to suppress sweating. Injections are painful and may require a topical anesthetic or nerve block for palmar hyperhidrosis. The axillae do not require anesthesia.
- Cervical–thoracic and lumbar sympathectomy are other effective methods to control palmoplantar hyperhidrosis.
- Local surgical ablation has been used to treat axillary hyperhidrosis.
- Microwave technology (miraDry) and lasers are used to decrease sweating in select patients.

Pediatric Considerations

- Emotional hyperhidrosis begins around puberty and improves with time.
- Boys and girls are affected equally, although girls more readily seek medical attention.

5 Psoriasis and Other Papulosquamous Diseases

James G. H. Dinulos

Psoriasis

Description

- Psoriasis is a common chronic inflammatory disorder caused in large part by abnormal T-lymphocyte function.
- Pink to red papules and plaques with thick white scale may be localized or widespread, involving the scalp, elbows, and knees.
- Psoriasis may be isolated to the scalp, nails, and skinfolds.
- Although psoriasis persists throughout life, patients may experience extended periods of remission.

History

- Prevalence worldwide is estimated to be 1% to 3% of the population.
- Psoriasis affects all age groups; onset is more common from 20 to 30 years and 50 to 60 years of age.
- Up to 90% of patients have a family history of psoriasis.
- Histocompatibility studies have shown HLA-Cw6 to be associated with up to a 25% risk for developing psoriasis and a 90% risk for early onset psoriasis.
- Many genetic loci have been linked to psoriasis, and *PSORS1* is thought to account for a 50% risk for psoriasis.
- Psoriasis is associated with an increased risk for anxiety, depression, obesity, diabetes, hypertension, lymphoma, myocardial infarction, and stroke.
- Flares of psoriasis may be triggered by local factors (skin injury, scratching), systemic factors (infections, especially *Streptococcus* and HIV), psychologic stress, medications (lithium, beta-blockers, interferon, and antimalarials).

Skin Findings

- Psoriasis may be grouped into distinct clinical patterns that are not mutually exclusive; patients may present with one pattern that evolves into another.

Chronic Plaque Psoriasis

- Chronic plaque psoriasis is the most common presentation.
- Red, sharply defined papules and plaques with thick white scale are seen and may be

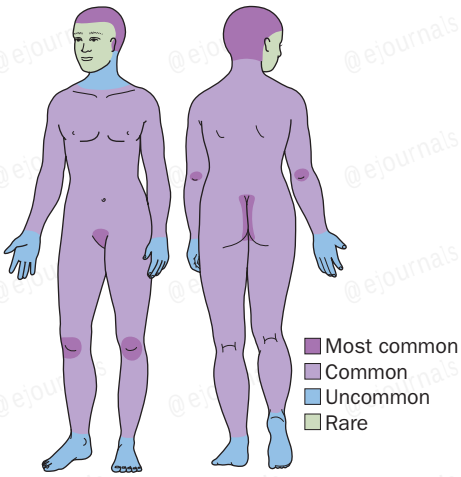

Fig. 5.1 Psoriasis distribution diagram.

Fig. 5.2 Psoriasis. Chronic plaque on the penis may be the only lesion of concern to the patient. Examine other likely areas of involvement, such as the scalp and gluteal cleft, to confirm the diagnosis. Reassure the patient that psoriasis is not contagious.

Fig. 5.3 Psoriasis. Extensive small chronic plaques with thick scaling on the lower leg. Note the interspersed areas of postinflammatory hypopigmentation of previously treated psoriasis plaques.

Fig. 5.5 Plaque psoriasis: the classical presentation. The thick red plaques have a sharply defined border and an adherent silvery scale.

Fig. 5.4 Psoriasis. Larger chronic plaques coalescing into geographic plaques. Such involvement responds well to ultraviolet light therapy.

Fig. 5.6 Plaque psoriasis. Plaques may become red and inflamed. Inflamed plaques need to be treated carefully with topical medication. All topical medications, except topical steroids, can aggravate these active lesions.

generalized with accentuation on the scalp, elbows, knees, and gluteal cleft.
- Firmly adherent scale bleeds when it is removed (Auspitz's sign).
- Aggressive mechanical removal of scale on the scalp may result in alopecia.

Guttate Psoriasis

- Guttate psoriasis is seen more commonly in children and young adults, who have been exposed to an upper respiratory virus or *Streptococcus pyogenes.*

Fig. 5.7 Plaque psoriasis. A fixed red plaque with a sharp border on the glans is a common presentation for psoriasis. It may be the only cutaneous lesion. The plaques often last for months and years. Topical steroids provide temporary relief but should not be used constantly. Most other topical medications are too irritating. Patients should be reassured that this disease is not contagious. Patients often misinterpret this disease as a yeast infection.

Fig. 5.8 Guttate psoriasis. Sudden appearance of numerous monomorphic psoriasis papules on the trunk is often triggered by streptococcal infection, particularly in children, adolescents, and young adults without prior history of psoriasis.

- Small round to oval red papules and plaques appear suddenly on the torso and extremities and have a tendency to resolve over a 6- to 12-month period.

Inverse (Intertriginous) Psoriasis

- Red, moist, and fissured plaques occur in the retroauricular folds, inframammary regions, axillae, inguinal creases, and intergluteal cleft.
- Inverse psoriasis is often confused with primary dermatophyte, candidal and streptococcal infection. These organisms may initiate a psoriatic flare.

Fig. 5.9 Guttate psoriasis. Closer inspection confirms guttate psoriasis and reveals firmly adherent white scale.

Fig. 5.10 Guttate psoriasis. The face, ears, and scalp may be involved with a flare of guttate psoriasis.

Fig. 5.11 Plaque psoriasis. Notice the thick plaque and scale. Plaque psoriasis and guttate psoriasis occuring simultaneously. These papules and plaques may be mildly itchy.

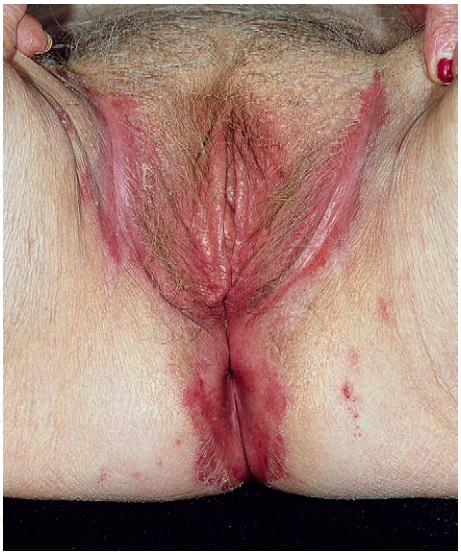

Fig. 5.12 Inverse psoriasis. Bright red scale involving the vulva, perineum, gluteal cleft are characteristic of inverse psoriasis. Note the absence of pustules. Pustules are typical of candida intertrigo.

Erythrodermic Psoriasis

- This severe form of psoriasis must be distinguished from other forms of cutaneous erythroderma, such as cutaneous T-cell lymphoma.
- Onset may be acute (drug-induced, systemic steroid withdrawal) or chronic from poorly controlled psoriasis.
- Patients may have skin tenderness, fever, weight loss, protein loss, and lymphadenopathy.

Pustular Psoriasis

- Pustular psoriasis is caused by intense inflammation resulting in sterile pustules.

Fig. 5.13 Scalp psoriasis. The posterior auricular folds should be treated with low potency topical corticosteroids and the scalp with higher potency topical corticosteroid shampoos, foams and solutions.

- Several clinical variants have been described, including generalized (seen in pregnancy, after infection, and systemic steroid withdrawal), localized (seen at the edge of an existing plaque), palmar/plantar (seen with smoking and possibly associated with bone lesions), and acral (seen on the distal portions of the toes and fingers with nail involvement).

Nail Disease

- Nail disease may occur in isolation, but most patients typically exhibit cutaneous signs of psoriasis. Signs of psoriatic nail disease include pits, nail whitening, friable nails, yellow spots ("oil spots"), splinter hemorrhages, thickened nail beds, and separation of the distal end of the nail plate from the nail bed (onycholysis).

Joint Disease

- Up to 30% of patients with psoriasis will develop psoriatic arthritis.

- Arthritis is more common in patients with widespread cutaneous involvement.
- A small number of patients develop psoriatic arthritis before the appearance of cutaneous psoriasis.
- Five clinical patterns have been described: monoarthritis and asymmetric oligoarthritis (most common form), distal interphalangeal, symmetric polyarthritis (similar to rheumatoid arthritis), mutilating arthritis, and spinal arthritis.

Laboratory

- Usually skin biopsy is not necessary to diagnosis psoriasis but should be considered before systemic therapy is administered.
- Primary providers should monitor cholesterol, blood sugars, and blood pressure because psoriatic patients are at risk for cardiovascular disease and metabolic syndrome.
- Throat cultures and antistreptolysin O titers should be performed in patients with guttate flares.
- Wet mounts and bacterial cultures should be performed in patients with inverse psoriasis or in patients who flare despite adequate topical or systemic therapy.
- In severe recalcitrant cases, evaluate for infection with HIV.

Fig. 5.16 Pustular psoriasis of the soles. Extensive involvement is painful. Systemic medication is sometimes required.

Fig. 5.14 Scalp psoriasis. Dense scale covering a part of or the entire scalp surface is highly characteristic of psoriasis. The scalp of all patients with psoriasis should be examined.

Fig. 5.17 Psoriasis of the soles is painful and responds well to systemic agents.

Fig. 5.15 Scalp psoriasis. Sometimes it is impossible to distinguish between scalp psoriasis and seborrheic dermatitis. The ears and faces of patients with seborrheic dermatitis are often involved.

Fig. 5.18 Psoriasis on the soles. Tinea may secondarily infect psoriasis and should be considered if psoriasis fails to respond to topical steroids.

Fig. 5.19 Psoriasis of the palms. This deep red, smooth plaque is painful.

Fig. 5.20 Pustular psoriasis. This rare form of psoriasis can be extensive and serious. It responds to cyclosporine, methotrexate, or acitretin.

Differential Diagnosis

- Seborrheic dermatitis
- Dyshidrotic eczema (hand, foot)
- Tinea capitis (scalp)
- Onychomycosis (nails)
- Intertrigo (candidal or streptococcal)
- Pityriasis rosea
- Drug eruption

Treatment

- Psoriasis is treated in a graded manner starting with topical therapy and progressing to phototherapy and finally to systemic therapy.
- Given the chronic relapsing nature of psoriasis, treatments are combined and rotated to minimize the toxicity of any one given treatment.

Topical Therapy

- Topical glucocorticoids are the mainstay of localized psoriasis.
- In general, psoriatic lesions on the scalp, torso, and extremities require more potent glucocorticoids (classes I–II), whereas lesions on the delicate areas of the face and intertriginous areas receive lower potency glucocorticoids (classes V–VI).
- Steroid-sparing medications (tar, retinoids, vitamin D analogs) are frequently combined with glucocorticoid to enhance their effectiveness and minimize side effects, such as skin thinning.
- An example of a regimen for plaque psoriasis on the elbows may include a vitamin D analog twice daily (e.g., calcipotriene cream, calcitriol ointment) during the week and a class I glucocorticoid twice daily during the weekends.
- Glucocorticoids may be compounded with tar in specialized compounding pharmacies.
- Calcipitriol-betamethasone diproprionate (Taclonex) is an example of a combination medication that is effective for psoriasis on the scalp, torso, and extremities.
- Triamcinolone acetonide injections (5–10 mg) effectively induce remission in many difficult-to-control psoriatic plaques.
- Some locations, such as the scalp and nails, may be more challenging to treat.

- Thick scale on the scalp may be gently removed with olive oil occluded with a warm, moist towel for 30 minutes. Scale must be gently removed to prevent alopecia.
- Derma-Smoothe oil is effective for more mild scalp psoriasis.
- Foams and solutions are easier to apply to the scalp than creams and ointments.
- Mildly affected nails may be treated with a class I topical glucocorticoid solution.
- More severely affected nails may be treated with triamcinolone acetonide injections (5–10 mg) into the nail bed.
- Generally, nail disease requires systemic therapy for improvement.

Phototherapy

- Phototherapy may be used as a solo therapy or in combination with topical or systemic agents.
- The most common treatment is narrowband ultraviolet B (311–313 nm), which has been shown to be highly effective.

Fig. 5.21 Erythrodermic psoriasis. Generalized intense inflammation can occur and often requires systemic medications for control.

Fig. 5.22 Pustular psoriasis. Pustules may coalesce, forming small "lakes of pus."

Fig. 5.23 Psoriasis pitting. Foci of inflammation of the proximal nail matrix results in the accumulation of parakeratotic cells on the nail surface. These are shed as the nail grows out, leaving depressions or pits in the nail surface.

Fig. 5.24 Psoriasis oil-spot lesion. Accumulation of parakeratotic debris and serum under the nail produces a yellow-brown stain under the nail.

Fig. 5.25 Psoriasis nail deformity. Inflammation of the proximal nail matrix causes surface deformity of the nail plate.

Fig. 5.26 Psoriatic onycholysis. Psoriatic inflammation of the skin at the fingertip causes distal nail plate separation. The picture can be identical to that seen with traumatic onycholysis.

- Patients require three treatments per week for 1 to 3 months. Many patients go on and off phototherapy for years.
- Tar, vitamin D analogs, retinoids (tazarotene cream or gel), and topical steroids enhance the effectiveness of phototherapy.
- The excimer laser (ultraviolet B, 308 nm) is effective for limited plaque psoriasis and is administered two to three times per week.

Fig. 5.27 Psoriasis onycholysis and nail deformity. Inflammation of various parts of the nail matrix produces a bizarre pattern of nail deformity. Clinical differentiation from onychomycosis is sometimes difficult.

- Other modalities include broadband ultraviolet B and A wavelengths (usually administered with psoralen).

Systemic Therapy

- Current systemic therapy may be divided into traditional and biologic therapy.
- Methotrexate, cyclosporine, and acitretin are the most widely used traditional systemic treatments for psoriasis.
- Methotrexate acts by inhibiting folic acid and is effective for all forms of psoriasis.
- Methotrexate is administered weekly through oral, subcutaneous, and intramuscular routes.
- Cyclosporine is a calcineurin inhibitor and effectively improves psoriasis quickly.
- Cyclosporine may be used to quickly improve more severe forms of psoriasis, such as pustular psoriasis and erythrodermic psoriasis.
- Acitretin is a systemic retinoid that is very effective for all forms of psoriasis, but is

used mostly for erythrodermic, pustular, and palmar/plantar psoriasis.
- Biologic treatments are immune modulators that target the T cell and cytokines involved in psoriasis.
- These agents are highly effective but are very expensive and thus are not accessible to many patients.
- Etanercept, infliximab, and adalimumab target tumor necrosis factor-alpha; ustekinumab targets p40 subunit of interleuin-12/23; secukinumab and ixekizumab target interleukin-17A. Brodalumab binds to the IL-17 receptor. Guselkumab targets interleukin-23.
- There are many targeted immunologic modulators in the pipeline for psoriasis.

Fig. 5.28 Psoriasis. Typically, treated psoriasis plaques clear in the center and then gradually improve at the periphery.

Fig. 5.29 Inflammatory plaque psoriasis may be painful. This active disease failed to respond to topical steroids, and methotrexate was started.

Fig. 5.30 Inflammatory plaque psoriasis. This plaque has partially responded to clobetasol cream. Topical steroids usually do not clear a plaque completely, and the disease typically returns after topical application is stopped.

Fig. 5.31 Inflammatory plaque psoriasis. Chronic inflammation of the palms is a difficult diagnostic problem. Psoriasis and eczema may have a similar appearance. Both are difficult to treat.

Fig. 5.32 Chronic plaque psoriasis may be asymptomatic. This patient was not uncomfortable and became discouraged with topical treatments. He was satisfied with using just moisturizers.

Fig. 5.33 Chronic plaque psoriasis. Gentle sunlight is an effective treatment. Sunburn can initiate a psoriatic flare.

Fig. 5.34 Psoriasis can occur at site of trauma (Koebner's phenomenon). This is psoriasis occurring on the donor site of a skin graft.

Seborrheic Dermatitis

Description

- Seborrheic dermatitis is a common, chronic, inflammatory condition characterized by pink to yellow plaques with waxy scale involving areas of the body with increased sebaceous glands including the scalp, central face, ears, and chest.
- *Malassezia furfur (Pityrosporum ovale)* is thought to cause seborrheic dermatitis.

History

- Seborrheic dermatitis occurs in all age groups.
- Infantile seborrheic dermatitis tends to resolve by 1 year of age.
- Approximately 5% of adults have seborrheic dermatitis.
- Men are affected more than women.
- Seborrheic dermatitis is more severe in patients with neurologic disorders (Parkinson's disease, stroke, and head trauma) and patients infected with HIV.

Skin Findings

- Pink to yellow papules and plaques with greasy scale involve scalp, central face, ears, and presternal areas. Characteristic locations are the eyebrows, the base of eyelashes (seborrheic blepharitis), nasolabial folds and paranasal skin, and external ear canals.
- May affect flexural skin, including the postauricular, inguinal, and inframammary folds as well as the anogenital area.

Laboratory

- Skin biopsy should be performed for atypical presentations.
- Fungal wet mount preparations should be considered for resistant cases.

Differential Diagnosis

- Rosacea
- Psoriasis
- Eczema

Treatment

- Adults tend to have a chronic course with seasonal remissions and exacerbations.
- Flares are precipitated by stress, fatigue, and climate changes.
- Mild to moderate facial seborrheic dermatitis may respond well to topical antifungals, such as ketoconazole cream or ciclopirox.

Pediatric Considerations

- Yellow, greasy adherent scale on the vertex of the scalp (cradle cap) with minimal underlying redness.
- Scale may accumulate, becoming thick and adherent over much of the scalp.
- Diaper area and axillary skin may become involved, often with redness that is more obvious than scaling.
- Secondary bacterial and candidal infection can occur.
- Infantile seborrheic dermatitis is easy to diagnose. Infants who do not respond to standard treatment measures can rarely have an underlying systemic illness such as Langerhans' cell histiocytosis or zinc deficiency.
- Infantile seborrheic dermatitis is usually a self-limited condition often not requiring treatment. Usually gentle removal of scale and a low-strength corticosteroid are sufficient to control infantile seborrheic dermatitis.
- Referral to a dermatologist is indicated for infants with severe recalcitrant seborrheic dermatitis or with widespread disease.

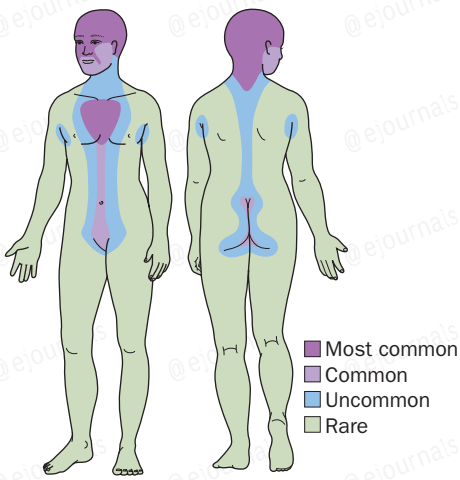

Fig. 5.35 Seborrheic dermatitis distribution diagram.

- Daily facial washing with antidandruff shampoo or soaps containing zinc pyrithione (ZNP) or selenium sulfide (Selsun) is effective. These shampoos and soaps are drying, and a light moisturizer is needed in most cases.
- Group VI or VII topical steroid creams or lotions (hydrocortisone or desonide) applied twice daily as needed are effective.
- Promiseb cream is a nonsteroidal treatment option that has anti-inflammatory and antifungal properties.

Fig. 5.36 Seborrheic dermatitis. Erythema and scaling may be extensive and extend beyond the nasolabial folds.

Fig. 5.37 The rash may extend beyond the nasolabial folds to involve the cheek.

Fig. 5.38 Seborrheic dermatitis. Scale of the lid margins occurs more often in children. The scales may irritate the conjunctiva.

Fig. 5.39 Seborrheic dermatitis. Patients with a propensity to develop seborrheic dermatitis will develop erythema and scale if they grow a beard. The disease will often clear if the hair is shaved.

Fig. 5.40 Seborrheic dermatitis. Dense patches of quadrangular scale occur in children. The scale adheres to the hair (tinea amiantacea). Scale should be gently removed with olive oil; vigorous removal may result in permanent hair loss.

Fig. 5.41 Seborrheic dermatitis of the ears usually requires group V topical steroids for control. Patients should pay special attention to drying the ears after bathing because moisture will flare seborrheic dermatitis.

Fig. 5.44 Seborrheic dermatitis. Crusted scaling of the eyelids responds to gentle removal with washcloth and mild cleanser.

Fig. 5.42 Seborrheic dermatitis. Active disease in all of the characteristic areas. The inflammation cleared with ketoconazole cream.

Fig. 5.45 Seborrheic dermatitis. Inflammation is more obvious than scaling in this patient with eyebrow involvement. Topical ketoconazole and intermittent topical desonide lotion will likely control this seasonal flare.

Fig. 5.43 Seborrheic dermatitis. A classical presentation for seborrheic dermatitis. Ketoconazole cream failed. A 7-day course of a group V topical steroid was effective. The patient was warned not to use topical steroids continuously on the face.

Fig. 5.46 Seborrheic dermatitis. Presternal faint plaques with thin, moist scale typical of a summertime flare.

- Tacrolimus 0.1% and pimicrolimus 1% applied twice daily are effective.
- Mild to moderate scalp involvement is best managed with frequent and extended shampooing with antidandruff shampoos.
- Effective formulations may contain ketoconazole (Nizoral), ciclopirox (Loprox), coal tar (Tarsum, T-Gel), salicylic acid (T-Sal), selenium sulfide (Selsun), and zinc pyrithione (Head & Shoulders).
- Dense, thick, adherent scale is removed by applying warm mineral or olive oil to the scalp and washing several hours later.
- For severe scalp involvement, 10% liquor carbonis detergens (LCD) in Nivea oil or Derma-Smoothe FS scalp oil (peanut oil, mineral oil, fluocinolone acetonide 0.01%) applied to the scalp at night effectively removes thick adherent scale. Wetting the scalp before application and using a shower cap increase absorption of the medication.
- Severe cases may require oral antifungal therapy to eradicate *M. furfur.*
- Antifungal therapy includes fluconazole 150 mg daily, or itraconazole 200 mg daily, for 1 or 2 weeks. Terbinafine is not effective.

Fig. 5.47 Seborrheic dermatitis. Postauricular involvement may be difficult to discern from psoriasis. In addition to shampoos, desonide lotion will control the itching and scaling.

Fig. 5.49 Seborrheic dermatitis. Erythema with more adherent greasy scale in this adolescent patient may require twice-daily washing and topical antifungal cream.

Fig. 5.48 Seborrheic dermatitis. Glabellar involvement with transparent scaling responds to daily washing with ZNP bar and intermittent use of group VI or VII topical steroid.

Fig. 5.50 Seborrheic dermatitis occurs on the presternal area. This eruption was controlled with ZNP bar soap (2% pyrithione zinc) and periodic treatment with a group V topical steroid.

Fig. 5.51 Seborrheic dermatitis. Very active inflammation with erythema and dense scale. Inflammation of this intensity usually responds to ciclopirox lotion (Loprox) or ketoconazole (Nizoral cream).

Fig. 5.52 Infantile seborrheic dermatitis begins on the scalp (cradle cap). There are well-defined red to salmon-colored plaques covered with greasy scale. They may descend to involve the face, trunk, and diaper area. Itching is minimal. Atopic dermatitis itches.

Fig. 5.53 Extensive infantile involvement of the scalp with crusted scale. Gentle débridement of scale is recommended with oil soak (e.g., Derma-Smoothe/FS) followed by washcloth with gentle shampoo or cleanser. Group VI topical steroids may then be used to control the inflammation.

Grover's Disease (Transient Acantholytic Dermatosis)

Description

- Grover's disease is a common inflammatory disorder characterized by mildly pruritic pink papules with a scant amount of white scale, occurring primarily on the torso.

History

- Grover's disease is most common in white men older than 40 years. Rash may flare with cold weather, sweating, heat, and friction.
- Grover's disease tends to be a chronic condition that persists for years.

Skin Findings

- Multiple pink pruritic papules with a small amount of rough scale occur on the central chest, back, and lumbar areas.

Laboratory

- Skin biopsy may help differentiate from folliculitis.

Differential Diagnosis

- Folliculiti
- Candidiasis
- Dermatitis herpetiformis
- Drug eruptions
- Viral exanthems
- Pityriasis rosea
- Miliaria rubra
- Insect bites
- Darier's disease

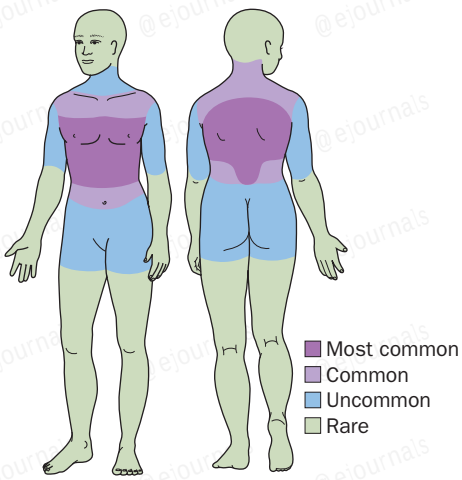

Fig. 5.54 Grover's disease distribution diagram.

Treatment

- Midpotency topical glucocorticoids, such as triamcinolone, help control itch and redness.
- Phototherapy may be used in combination with topical glucocorticoids.
- Oral antihistamines are used to control itching.

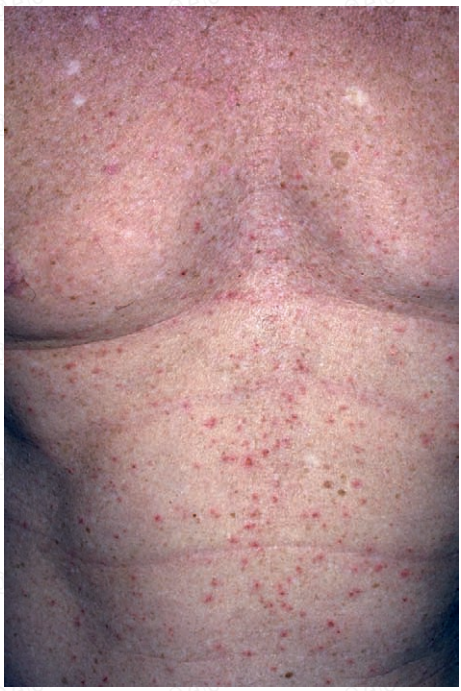

Fig. 5.55 Grover's disease may cover wide areas of the chest and abdomen. Itching is common, but not universal.

Fig. 5.56 Grover's disease. Pink-brown papules with a scant amount of scale are characteristic.

Pityriasis Rosea

Description

- Pityriasis rosea is a common rash characterized by oval pink to red papules and plaques with a distinctive collarette of scale, occurring primarily on the trunk.

History

- More than 75% of patients are between 10 and 35 years of age.
- Many patients report a mild prodrome or upper respiratory illness within a month of onset.
- Multiple cases occurring seasonally in the spring and fall point to a viral cause, although this has not been confirmed.
- Limited outbreaks have occurred in close quarters, such as fraternity houses and military barracks.

Skin Findings

- The first lesion ("herald patch") appears suddenly and asymptomatically, often on the chest or back.
- The typical lesion is an oval plaque, which develops a thin collarette of scale just inside the edge.
- One to 2 weeks later, numerous oval pink to brown papules and plaques develop on the trunk and proximal extremities. The long axis of the plaques follow skin tension lines, reminiscent of drooping pine branches.
- Lesions usually clear spontaneously in 4 to 12 weeks, without scarring.
- In dark skin, postinflammatory pigmentary change may take months to resolve.

Pediatric Considerations

- Children often have numerous lesions that can have varying morphologies: purpuric, vesicular, and papular.
- Children can have lesions that predominate in the groin, elbows, and knees (inverse pityriasis rosea).

Laboratory

- Skin biopsy is not usually necessary but is helpful in atypical cases.
- Potassium hydroxide wet mount is useful to rule out fungal infection.
- A serologic test for syphilis should be considered in the right clinical setting, especially if lesions are also present on the palms and soles.

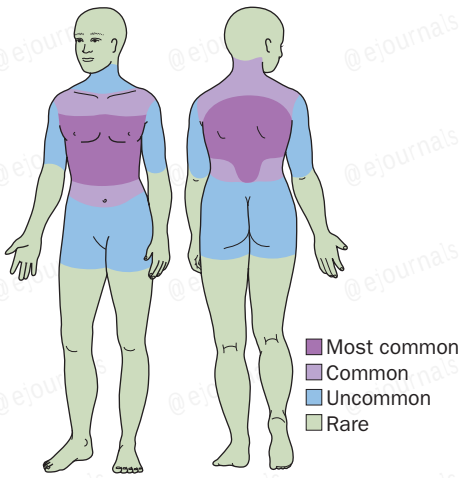

Fig. 5.57 Pityriasis rosea distribution diagram.

Fig. 5.58 Pityriasis rosea. The first lesion is usually the largest. It is called the *herald patch*. It can be located anywhere but is typically found on the trunk. Here the herald patch is found on the left breast. Lesions that follow are smaller and usually confined to the trunk. Concentration of lesions in the lower abdominal and pubic area is highly characteristic of pityriasis rosea. Exposure to sunlight is an effective treatment. Here the lesions only appear on unexposed skin.

Fig. 5.59 Pityriasis rosea. An extensive case in a typical distribution with lesions in the lower abdominal region. Here lesions are also found on the upper arms. It is very unusual to find lesions on the forearms or the lower legs. Most patients experience little or no itching.

Fig. 5.61 Pityriasis rosea. Extensive case extending onto the neck as typical oval pityriasis rosea plaques.

Fig. 5.60 Pityriasis rosea. Lower abdominal involvement with an unusual degree of inflammation. Collarette scaling is seen in most plaques. Ultraviolet therapy would likely help this patient.

Fig. 5.62 Pityriasis rosea. A classical image of the primary lesion of pityriasis rosea. The thin collarette of scale is within the plaque and surrounded by an inflammatory border.

Differential Diagnosis

- Tinea corporis
- Tinea versicolor
- Secondary syphilis
- Drug eruption
- Guttate psoriasis

Treatment

- Mentholated lotions (Sarna) or sprays (Eucerin Anti-Itch) are helpful for itching.
- Group V topical steroids and oral antihistamines provide some relief.
- Ultraviolet B light, either from natural sunlight or administered in metered doses by a dermatologist, hastens resolution.
- A 2-week course of erythromycin has been effective in some patients.

Pearls

- Consider referral to a dermatologist when the lesion morphology is variable, when the

lesions are more extensive than expected, or when the eruption is lasting longer than expected. A small percentage of cases are thought to be recurrent and should be referred for skin biopsy.

- The herald patch is characteristic of pityriasis rosea but is often misdiagnosed as tinea.
- Pityriasis may be indistinguishable from secondary syphilis.

Fig. 5.63 Pityriasis rosea. Highly active disease involving the neck, trunk, and extremities. The circular scale supports the diagnosis. Erythromycin 250 mg taken every day for 2 weeks was effective.

Fig. 5.64 Pityriasis rosea. A ring of tissue-like scale (collarette scale) remains attached within the border of the oval plaque. This is almost pathognomonic of pityriasis rosea. The scale appears at the border with fungal infections.

Fig. 5.65 Pityriasis rosea. Lesions are typically concentrated in the lower abdomen and groin. Eruptions may be intense and widespread. The circular scale is a clue to the diagnosis.

Fig. 5.66 Pityriasis rosea. In dark-skinned patients and children, pityriasis rosea can occur on the arms and legs and spare the back (inverse pityriasis rosea).

Lichen Planus

Description

- Lichen planus is an idiopathic papulosquamous disorder characterized by itchy pink to purple papules and plaques, occurring primarily on the scalp, extremities, nails, and mucous membranes.

History

- Most patients develop the disorder between 30 and 60 years of age.
- Lichen planus is rare in children younger than 5 years and in elderly people.
- Up to 10% of patients have a family history of lichen planus.
- Most patients with cutaneous disease show evidence of mucosal involvement.
- The cause is unknown, but lichen planus may be a T-cell–driven autoimmune disease.
- Lichen planus may be associated with hepatitis C and many medications.

Skin Findings

- The primary lesion is a 2- to 10-mm flat-topped papule with an irregular, angulated border (purple polygonal papules).
- New lesions are pink to white, but over time they become purple and sharply defined.
- Surface shows a lacy reticulated pattern of whitish lines (Wickham's striae).
- New lesions may develop in areas of injury (Koebner's phenomenon).
- There are several clinical forms.

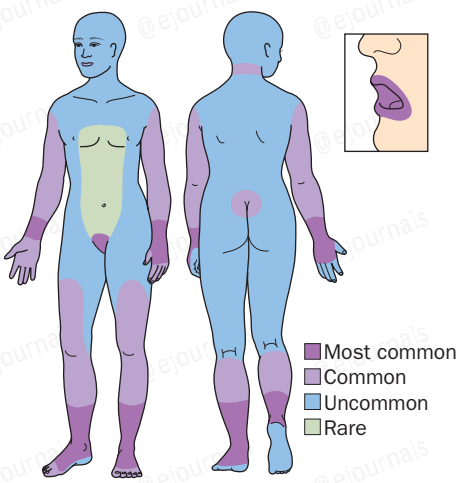

Fig. 5.67 Lichen planus distribution diagram.

Fig. 5.68 Lichen planus. The primary lesion is a flat-topped papule with an irregular, angulated border (polygonal papule).

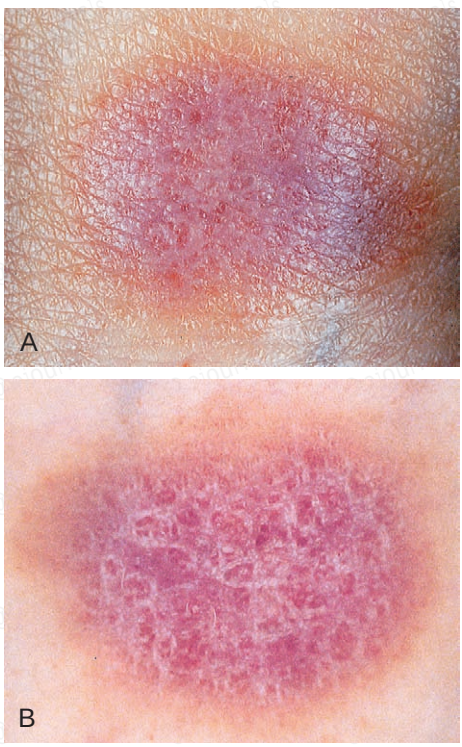

Fig. 5.69 Lichen planus. **A,** Close inspection of the surface shows a lacy reticular pattern of crisscrossed whitish lines (Wickham's striae). **B,** High power view with oil and a dermatoscop shows accentuated Wickham's striae.

Fig. 5.70 Lichen planus. White plaques are located on the buccal mucosa. The classical presentation is a lacy, net-like pattern.

Fig. 5.71 Lichen planus. Notice the white lacy pattern. There is no scale as would be seen in actinic chelitis, which commonly affects the lower lip.

Fig. 5.72 Lichen planus. The white lacy reticular pattern is present on the glans and shaft. Lesions are asymptomatic.

Fig. 5.73 Lichen planus. Lesions are concentrated about the wrists and ankles. Itching varies in intensity and may not be present.

Fig. 5.74 Lichen planus may be linear in a zosteriform pattern.

Fig. 5.75 Lichen planus: flat-topped, thick plaques with thin scale on an extremity. Such lesions often require intermittent use of a potent topical steroid.

Fig. 5.76 Lichen planus. Inflammation is obscured in dark-skinned patients by hyperpigmentation.

Fig. 5.77 Lichen planus. Inflammation may be obscured in dark-skinned patients by hyperpigmentation. Rely on the morphology and distribution of lesions to make the diagnosis.

Fig. 5.78 A, Lichen planus on the back of the hand with faint Wickham's striae over dermal inflammation. **B,** Under immersion oil, the epidermal Wickham's striae stand out above the underlying dermal inflammation.

Fig. 5.79 Lichen planus. Classical image of lichen planus papules on the ankle. Itching may be unremitting.

Fig. 5.80 Lichen planus. Typical flat-topped papules in the wrist. Note the linear arrangement of some papules suggesting both excoriation and Koebner's phenomenon as new lesions are produced by surface trauma.

Fig. 5.81 Hypertrophic lichen planus. Thick red-brown to purple plaques on the pretibial surface. These lesions respond well to intralesional triamcinolone acetonide.

Fig. 5.82 **A,** Larger plaques of lichen planus on the wrist before treatment with topical steroids. **B,** Follow-up of same patient with lichen planus. The plaques are reduced in height and diameter, although postinflammatory hyperpigmentation persists.

Fig. 5.83 Lichen planus. Coalescing papules on the pretibial area forming a hypertrophic plaque with hyperkeratosis and focal crusting. Squamous cell carcinoma may occur with longstanding lichen planus.

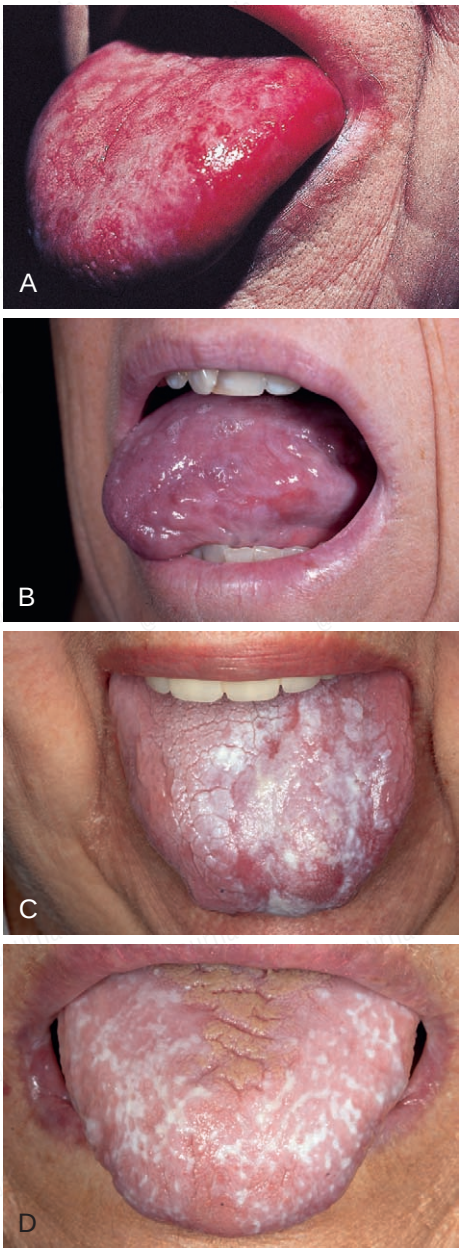

Fig. 5.84 A, Lichen planus of the tongue. The surface is red and smooth with loss of papillae. White striae are an almost constant feature. *Candida* has a similar appearance. **B,** The tongue is atrophic and scarred from long-term activity. **C,** Hypertrophic white plaques look like chronic *Candida* infection. **D,** Linear white bands cover the entire tongue.

Papular Lichen Planus

- The most common clinical presentation is papular.
- Pruritic papules are located on the flexor surfaces of the wrists and forearms, the ankles, and the lumbar region.

Hypertrophic Lichen Planus

- Lesions that persist become thicker and darker red.
- Most often they are on the pretibial surfaces.
- Papules aggregate into different patterns.
- Vesicles or bullae may appear.
- Persistent brown staining develops after the lesions resolve.
- Squamous cell carcinoma may arise within hypertrophic lichen planus.

Follicular Lichen Planus

- Follicle-based papules appear on the scalp.
- Permanent hair loss can occur with associated marked scarring (scarring alopecia).

Mucosal Lichen Planus

- Most common form is nonerosive, which produces a white lacy pattern.
- Mucosal lichen planus may become erosive and extremely painful.
- Oral lesions primarily involve the buccal mucosa and lateral edge of the tongue.
- Mucosal lichen planus may involve the mucosal lip but rarely extends beyond the vermillion border.
- The penis and vulva may be involved, with intense itching and burning, marked mucosal fragility, and erythema.

Nail Lichen Planus

- Ten percent of patients with cutaneous lichen planus show nail changes, but nail changes may be present in the absence of cutaneous disease.
- Characteristic nail findings include thinning, longitudinal ridging, and fissuring.
- Untreated nail lichen planus may lead to scar and pterygium formation.

Laboratory

- Skin biopsy may assist in distinguishing between lupus and lichenoid drug reaction.

- Severely affected patients should be tested for hepatitis C virus infection.
- Patch testing may be helpful in the evaluation of oral lichen planus because select patients are allergic to metallic dental restorations.

Differential Diagnosis

- Papular eczema
- Psoriasis
- Lichen simplex chronicus
- Cutaneous lupus
- Pemphigus

Treatment

- Sedating antihistamines (hydroxyzine 10–25 mg every 4 hours) are effective to control itch.
- Group I or II topical glucocorticoids are required to control lichen planus.
- Intralesional triamcinolone acetonide (Kenalog 5–10 mg/mL) is very effective for thicker plaques.
- For oral lichen planus, high-potency glucocorticoid (ointments or orabase) and tacrolimus applied twice daily are effective to control inflammation.
- Narrow-band ultraviolet B should be considered for widespread lichen planus.
- Systemic glucocorticoids, methotrexate, cyclosporine, and mycophenolate mofetil should be considered for severe lichen planus.

When to Refer

- Scarring alopecia, erosive mucosal involvement, and refractory cases should be referred to a dermatologist for management.

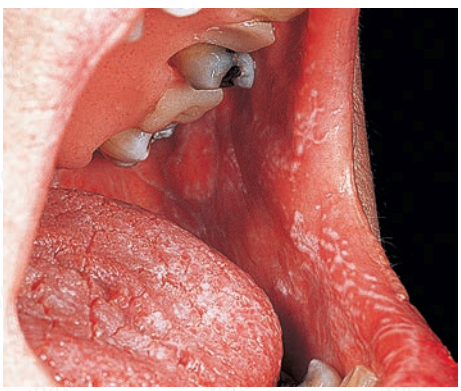

Fig. 5.85 Mucous membrane lichen planus. A lacy white pattern is present on the buccal mucosa.

- Gastroenterology referral should be considered for hepatitis C infection management.

Pearls

- The five Ps of lichen planus are *p*ruritic, *p*lanar (flat-topped), *p*olygonal, *p*urple, and *p*apules.
- White lacy patches of the oral mucosa are virtually diagnostic of oral lichen planus.

Fig. 5.86 Generalized lichen planus. Papules are larger and are confluent in the lower back region.

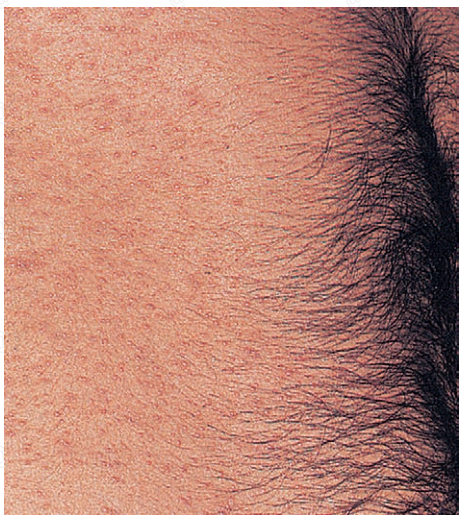

Fig. 5.87 Generalized lichen planus. Pinpoint papules are numerous and widespread. The differential diagnosis includes a lichenoid drug reaction.

Fig. 5.88 Localized lichen planus. Early lesions are present on the wrist, which is a common site for localized lichen planus.

Fig. 5.89 Hypertrophic lichen planus occurs on the lower legs. These plaques have a violaceous hue and are thick. Itching may be intense.

Fig. 5.90 Bullous lichen planus. Lichen planus may present with blistering.

Fig. 5.91 Erosive vaginal lichen planus. Women present with itching, soreness, and dyspareunia. Topical clobetasol is effective to treat erosive vaginal lichen planus.

Lichen Sclerosus

Description

- Lichen sclerosus is an uncommon inflammatory disorder, producing ivory-white indurated plaques and scars in the genital skin. Extragenital lichen sclerosus is less common.

History

- The female-to-male ratio is 10:1.
- Lichen sclerosus can occur at any age but is more common in women older than 60 years and prepubertal girls between 8 and 13 years of age.
- Vulvar pruritus, dysuria, or dyspareunia are common complaints.
- Squamous cell carcinoma develops in 3% of genital lesions.

Skin Findings

- The primary lesion is an ivory-white, atrophic papule with a faint-pink rim.
- Lichen sclerosus may be very itchy and interfere with daily activities and sleep.
- On the skin, flat-topped, slightly raised papules coalesce into small oval plaques with a dull or glistening, smooth, white, atrophic, wrinkled surface.
- Focal subsurface hemorrhage may be seen among plaques.
- Keratotic follicular plugs appear on the surface (delling).
- On mucosal surfaces, papules are fragile, atrophic, white, and glistening with a wrinkled surface.
- Penile lesions (balanitis xerotica obliterans) favor the glans and coronal sulcus but may extend to the shaft.
- Surface trauma leads to focal subepidermal hemorrhages and erosions.
- Atrophy leads to phimosis of the foreskin with pain on retraction of the foreskin or erection.
- The urethral meatus may become stenotic, and malignant degeneration may occur.
- Vulvar papules tend to coalesce, forming a white atrophic plaque with an hourglass shape, which encircles the vagina and anus.
- Focal purpura is common, and mucosal lesions may erode.

Laboratory

- Biopsy is helpful in early cases and for areas suspicious for squamous cell carcinoma.
- Secondary candidiasis can occur as a consequence of treatment, and a potassium hydroxide examination should be considered.

Differential Diagnosis

- Morphea and lichen sclerosus are similar on the skin (rarely both conditions may be present in some patients, although the presence of mucosal lesions favors a single diagnosis of lichen sclerosus)
- Lichen planus and pemphigus vulgaris (especially for erosive mucosal lesions)
- Lichen simplex chronicus (vulvar involvement from scratching)
- Allergic contact dermatitis (typically fragrance allergy from personal hygiene products or steroid allergy from prior treatment)

Pediatric Considerations

- Purpura of the vulva is an occasional manifestation of lichen sclerosus in prepubertal girls.
- This may be misdiagnosed as child abuse, thus lichen sclerosus should be carefully ruled out in such cases.
- Prepubertal cases usually resolve without sequelae, other than hyperpigmentation.

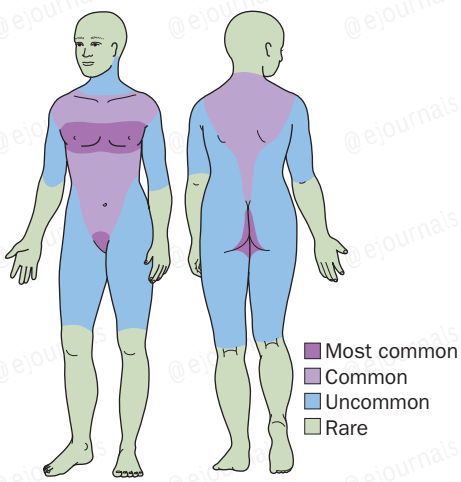

Fig. 5.92 Lichen sclerosus distribution diagram.

- Extramammary Paget's disease (should be considered for chronic anogenital itching with erosions)
- Steroid-induced atrophy (can be confused with lichen sclerosus)

Treatment

- The goal of treatment is to prevent scarring and squamous cell carcinoma.
- Patients should used gentle cleansers such as Cetaphil and moisturize with a light moisturizer.

Fig. 5.93 Lichen sclerosus. Early lesions are ivory-colored, flat-topped, slightly raised papules with follicular plugs.

Fig. 5.94 Lichen sclerosus. The epidermis is thin and atrophic and gives the appearance of wrinkled tissue paper when compressed.

Fig. 5.95 Lichen sclerosus. This is the classical presentation for a lesion that has been present for months. The plaque is white, firm, and dense. Large follicular plugs are present in the center.

- Women should avoid fragranced feminine hygiene products and scented toilet paper.
- Clobetasol propionate 0.05% ointment is effective for vaginal and penile disease in adults. Intralesional triamcinolone acetonide (Kenalog, 2.5–5.0 mg/mL) may be useful for unresponsive areas.
- Extragenital lichen sclerosus responds well to ultraviolet B phototherapy.

Pearls

- Chronic vulvar itching in the absence of infection should raise the suspicion of lichen sclerosus.
- Consider lichen sclerosus to be a precancerous condition requiring regular follow-up and biopsy of areas suspicious for malignant change.

Fig. 5.96 Lichen sclerosus. Symmetric vulvar involvement is seen in this patient who complained of intense itching and dyspareunia.

Fig. 5.97 Lichen sclerosus. A white atrophic plaque encircles the vagina and rectum (hourglass). The skin is fragile and easily erodes.

Fig. 5.98 Lichen sclerosus. The glans is smooth, white, and atrophic. Erosions are present on the prepuce.

Fig. 5.99 Lichen sclerosus. There is diffuse sclerosis of the glans and shaft. Several linear erosions are present.

Fig. 5.100 Lichen sclerosus in a prepubertal child. Notice the vaginal, perineal, and perianal distribution (figure-eight pattern). This child responded nicely to clobetasol ointment.

Pityriasis Lichenoides et Varioliformis Acuta and Pityriasis Lichenoides Chronica

Description

- Pityriasis lichenoides et varioliformis acuta (PLEVA) and pityriasis lichenoides chronica (PLC) result from T-cell infiltrates that produce vesicles, pustules and crusts (PLEVA), and scaly papules and plaques (PLC).
- PLEVA and PLC are thought to represent two ends of a disease spectrum, but many patients have mixed manifestations.

History

- The etiology is unknown but may be an immune response to an infectious agent or drug.
- PLEVA and PLC are more common in pediatric patients and more common in males.
- PLEVA may be confused with varicella because there are lesions in various stages of healing, but patients with PLEVA have a more protracted course, lasting months.
- Patients with PLEVA may become febrile and develop widespread ulcerations that result in scarring.

Skin Findings

- PLEVA and PLC occur in crops of round 2- to 8-mm red-brown papules, singly or in clusters.
- Papules have a violaceous hue and adherent thin scale.
- PLEVA lesions become vesicular and undergo hemorrhagic necrosis, usually within 2 to 5 weeks, often leaving postinflammatory hyperpigmentation. Depending on skin type, dyspigmentation can last many months.
- Lesions favor the trunk, thighs, and proximal extremities; face, scalp, palms, and soles are involved in approximately 10% of cases.
- PLC tends to be chronic, with many crops of lesions recurring over several months or years.
- PLC papules are usually asymptomatic, although mild itching may occur.

Laboratory

- Skin biopsy confirms the diagnosis.
- Gene rearrangement studies demonstrate T-cell clonality in some patients, suggesting a relationship to lymphomatoid papulosis and cutaneous T-cell lymphoma.

Differential Diagnosis

- Pityriasis rosea (also favors the trunk; lesion morphology is similar to chronic form)
- Lymphomatoid papulosis (lesions may undergo necrosis like those of the acute form)
- Insect bite reactions and scabies (may be confused with acute form)
- Varicella lesions: these occur in crops, with or without systemic symptoms

Treatment

- Oral antihistamines, such as hydroxyzine, are helpful to control itch. Oral erythromycin may produce a remission in some acute cases at a dose of 30 to 50 mg/kg daily over several weeks.
- Phototherapy with narrow-band ultraviolet B, tetracyclines, methotrexate, oral corticosteroids, and dapsone may be helpful for more severe cases.

Fig. 5.101 Lichen sclerosus. Sclerosis is limited to the glans. Note the ivory-white color of the glans.

Fig. 5.102 Pityriasis lichenoides et varioliformis acuta (PLEVA). Crops of red to brown papules can become hemorrhagic, pustular, or necrotic. Acute exacerbations are common, and the disease may wax and wane for months or years.

Fig. 5.103 Pityriasis lichenoides chronic (PLC). Children may have asymtomatic pink scaly papules that come and go for years.

Fig. 5.104 Pityriasis lichenoides et varioliformis acuta (PLEVA). Lesions in various stages of healing are seen similar to varicella.

Fig. 5.105 Pityriasis lichenoides et varioliformis acuta (PLEVA). A generalized eruption lasts weeks or months, unlike varicella.

6 Bacterial Infections

Kathryn A. Zug

Impetigo

Description

- Impetigo is a common, highly contagious, superficial skin infection produced by *Streptococcus pyogenes, Staphylococcus aureus,* or a combination of both bacteria.
- Bullous impetigo and nonbullous impetigo represent two clinical forms of the disease.
- *S. aureus* is the cause in about 80% of cases, and group A streptococcus in 20% to 30%.

History

- Impetigo may occur after a minor skin injury, such as an insect bite, or within lesions of atopic or another dermatitis; it often develops on normal skin.
- Children in close physical contact with one another have a higher rate of infection.
- Responsible staphylococci may colonize the nose and serve as a reservoir for skin infection.
- Warm, moist, humid climates and poor hygiene predispose to this condition.

Skin Findings

- Lesions may be localized or widespread. Impetigo is common on the face.

Bullous Impetigo

- Thin-roofed bullae may turn from clear to cloudy. Bullae collapse quickly, leading to an inner-tube–shaped rim with a central thin, flat, honey-colored, stuck-on crust.
- Lesions enlarge and often coalesce. There is minimal surrounding erythema. The thick crust accumulates in longer-lasting lesions.
- Lesions are found in all stages of evolution. Adenopathy may be mild.

Nonbullous Impetigo (Crusted)

- Vesicles or pustules rupture, exposing a red and moist base. A tinea-like scaling border forms as the round lesions enlarge.
- The firmly adherent crust is honey-yellow to white-brown in color; it accumulates as the lesion extends radially, and there is little surrounding erythema.
- Satellite lesions appear beyond the periphery.

Nonskin Findings

- Systemic symptoms are infrequent.
- Lesions are generally asymptomatic and painless.
- The incidence of acute nephritis is between 2% and 5%; in the presence of a nephritogenic strain of streptococci, the rate varies between 10% and 15%.
- Rheumatic fever has not been reported as a complication of impetigo.
- *S. aureus* is a common infection with potential serious complications in people infected with HIV. Recurrence after therapy is common.

Laboratory

- Cultures of lesions will reveal *S. aureus* or group A streptococcus. Group B

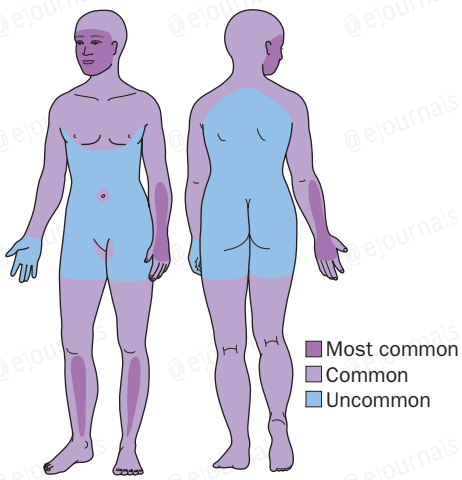

Fig. 6.1 Impetigo distribution diagram.

Fig. 6.2 Bullous impetigo. Huge lesions with a glistening eroded base and a collarette of moist scale.

Fig. 6.4 Rounded eroded and crusted plaques on the face of a child with bullous impetigo. Several lesions have typical honey-colored crust.

Fig. 6.3 Bullous impetigo. Large extensive lesions. Annular, eroded plaques with a peripheral collarette of scale.

Fig. 6.5 Excoriation of insect bites resulted in a secondary infection with impetigo. The infection was localized and responded to mupirocin ointment.

streptococcus may cause impetigo in the newborn. Sensitivity information is useful given the increasing incidence of antibiotic resistance and methicillin-resistant *S. aureus.*

Differential Diagnosis

- Perioral dermatitis
- Allergic contact dermatitis
- Herpes simplex and herpes zoster
- Pemphigus foliaceus and pemphigus vulgaris
- Tinea infection

Course and Prognosis

- The disease is self-limited, but if untreated, it may spread and last for weeks or months. Systemic complications are uncommon.
- Ecthyma (deeper, dermal infected lesions) may result from chronic, untreated impetigo infection and is most common on the leg. There is an increased risk for pyoderma, folliculitis, cellulitis, lymphadenitis, and ecthyma in carriers of *S. aureus* or group A streptococcus.

Treatment

- For limited, localized infections of nonbullous impetigo due to *S. aureus* or *S. pyogenes,* Mupirocin 2% ointment or cream (Bactroban) is used three times a day for 10 days. Retapamulin ointment (Altabax) used two times a day for 5 days is an alternative.
- For widespread infections, especially bullous impetigo, oral antibiotics are administered.

Consider also if athletic team involvement, child care groups, or multiple family members are affected. Culture and sensitivity are important. Empiric initial antibiotic therapy, such as dicloxacillin 250 mg or cephalexin (Keflex) 250 mg, is prescribed four times a day for 5 to 10 days. Pediatric doses are cephalexin 25 to 50 mg/kg/day divided two daily for 10 days, cefadroxil 30 mg/kg/day in two divided doses, dicloxacillin 12.5 mg/kg orally daily in four divided doses, or amoxicillin plus clavulanate 7.5 to 15 mg/kg (500 mg maximum) orally every eight hours for 5 days. Antibiotic-resistant staphylococci are a concern with oral erythromycin. For penicillin-allergic patients, azithromycin given over 5 days (500 mg on day 1 and 250 mg on days 2–5) or clarithromycin 250 to 500 mg twice daily for 10 days may be effective. Alternatives in community-acquired methicillin-resistant *S. aureus* (CA-MRSA) infections include clindamycin or doxycycline in children older than 8 years when bacterial isolate is sensitive.

- For recurrent impetigo, the presence of *S. aureus* is sought; the most common sites are the nares. Less commonly, it can be found in the perineum, axillae, and toe webs.
- Recurrent disease may be stopped with mupirocin 2% ointment to nares twice a day for 5 days. This course is repeated monthly for several months to eradicate nasal carriers of *S. aureus.*
- For recurrent infections consider bleach baths (soak for 5 to 10 minutes two or three times per week in diluted bleach—¼ cup regular bleach in a half tub of water).

Discussion

- *S. aureus* transiently colonizes the nares of 20% to 40% of healthy people and the skin of atopic individuals.
- Bullous impetigo is primarily a staphylococcal disease due to phage group II, type 71. It occurs most commonly in young children and newborns.
- Nonbullous impetigo was once thought to be primarily a streptococcal disease, but staphylococci are isolated from most lesions of bullous and nonbullous impetigo.
- An epidermolytic toxin produced at the site of infection, most commonly by staphylococci of phage group II, causes intraepidermal cleavage below or within the stratum granulosum, resulting in bulla formation in bullous impetigo.
- Guttate psoriasis is an uncommon sequela of impetigo.

Pediatric Considerations

- Impetigo is the most common bacterial skin infection of children.
- For localized impetigo, topical therapy with mupirocin (Bactroban) is generally well accepted by children.
- For widespread impetigo, systemic antistaphylococcal or antistreptococcal antibiotics (cephalexin 25 mg/kg/day in four divided doses for 7 days in children). Use culture and sensitivity when possible.
- Rarely, poststreptococcal glomerulonephritis may follow impetigo, typically 1 to 5 weeks after infection, and most commonly in children aged 2 to 4 years.
- Group A streptococcal serotypes associated with nephritis can be determined and are most commonly M-T serotypes 2, 49, 55, 57, and 60.
- Serious secondary infections (e.g., osteomyelitis, septic arthritis, pneumonia) may follow seemingly trivial superficial infections in infants.
- For recurrent impetigo, antibacterial soaps used twice daily are useful adjuncts.
- Bacterial culture can be helpful to evaluate for carrier state (nares) and resistant organisms (MRSA).

Fig. 6.6 Glistening, eroded patch with honey-colored crust in the nasolabial fold.

Fig. 6.7 Impetigo. Extensive honey-colored crusting and erythema on the upper and lower lips. Impetigo is

Fig. 6.8 Bullous impetigo. Lesions are present in all stages of development. Bullae rupture, exposing a lesion with an eroded surface and peripheral scale.

Fig. 6.9 A yellow crusted scaling border forms as the round patches enlarge.

Fig. 6.10 Small round macule with yellow crust at the nasal vestibule.

Fig. 6.11 Nonbullous impetigo. Extensive lesions that disseminated after treatment with topical steroid. The tip off are the multiple areas of erosion and crusting.

Cellulitis

Description

- Cellulitis is an infection of the dermis and subcutaneous tissues characterized by fever, erythema, edema, and pain.

History

- Localized pain and tenderness occur for a few days before presentation.
- The most susceptible populations are people with diabetes, cirrhosis, poor lymphatic circulation (i.e., postmastectomy), renal failure, malnourishment, and HIV. Patients who have cancer and are on chemotherapy or who abuse intravenous drugs and alcohol are also at increased risk.
- Cellulitis typically occurs near surgical wounds and trauma sites (e.g., bites, burns, abrasions, lacerations, and ulcers).
- It may develop in apparently normal skin or at sites of other dermatoses.
- Recurrent episodes occur with local anatomic abnormalities that compromise the venous or lymphatic circulation (e.g., chronic stasis dermatitis).
- The pinna and lower legs are particularly susceptible to recurrence.
- Picking skin and transfer of bacteria from fingernails into minor skin abrasions may be an important source.

Skin Findings

- A pre-existing lesion, such as an ulcer or erosion, may act as a portal of entry for the infecting organism.
- Athlete's foot may be a common predisposing condition for cellulitis of the lower extremities.
- An expanding red, swollen, tender, or painful plaque with an indefinite border may cover a small or wide area. Skin appears tight. Patient may have nausea, chills, shaking.
- Palpation produces pain, but rarely crepitus.
- Vesicles, blisters, hemorrhage, necrosis, or abscesses may occur.
- Regional lymphadenopathy sometimes occurs; lymphangitis and adenitis are common with infection with *S. pyogenes.*
- Repeated attacks on the legs can impair lymphatic drainage, leading to chronically swollen legs.
- The end stage of repeated infection of the leg includes dermal fibrosis, lymphedema, and epidermal thickening. This is known as *elephantiasis nostras.*

Laboratory

- Mild to moderate leukocytosis and a mildly elevated erythrocyte sedimentation rate may be present.
- Cellulitis without abscess is most often caused by a group A streptococcus. Many other bacteria, including *S. aureus,* can cause cellulitis. Less common causative organisms include *Erysipelothrix rhusiopathiae* (erysipeloid) in fish, poultry, meat, or hide handlers; *Aeromonas hydrophila* after swimming in fresh water; *Vibrio* species after swimming in salt water or exposure to raw seafood drippings; *Pasteurella multocida* from an animal bite or scratch.
- Culture of the lesion is a more predictable source of information than needle-aspirate cultures.

Differential Diagnosis

- Stasis dermatitis
- Thrombophlebitis
- Deep venous thrombosis
- Contact dermatitis
- Erythema nodosum

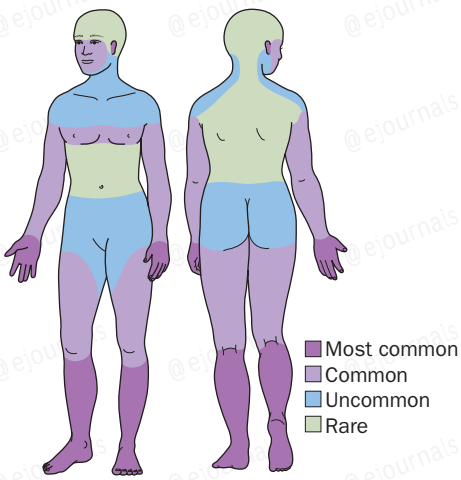

Fig. 6.12 Cellulitis distribution diagram.

Treatment

- Elevation of the affected limb assists with drainage and will hasten recovery. Rest with elevation of the affected limb is advised.
- Empiric treatment with antibiotics aimed at staphylococcal and streptococcal organisms is appropriate because it is difficult clinically to distinguish between streptococcal and staphylococcal infections.
- MRSA and macrolide- or erythromycin-resistant *S. pyogenes* can complicate management.
- If the case is not severe and there are no signs of systemic infection, treat with a semisynthetic penicillin (dicloxacillin 500–1000 mg orally every 6 hours, amoxicillin–clavulanate 875/125 mg twice daily or 500/125 mg three times daily), a cephalosporin (cephalexin 500 mg four times daily), or clindamycin 300 mg orally four times a daily. Reserve fluoroquinolone (levofloxacin) use for gram-negative organisms documented by culture.
- Cellulitis adjacent to an abscess has a high risk for MRSA strains. Most CA-MRSA strains are sensitive to trimethoprim–sulfamethoxazole, doxycycline 100 mg two times a day, and clindamycin 300 mg by mouth three to four doses daily.
- The mean time for healing after treatment is initiated is 12 days.
- Most cases improve when the patient is on simple oral antibiotic therapy for 5 days. Nonresponding cases require re-evaluation, consideration of infectious disease consultation, and intravenous antibiotics.
- Severe infections may require hospitalization and intravenous antibiotics. Intravenous empiric therapy with coverage for group A streptococci and *S. aureus* is cefazolin 1 g every 8 hours or nafcillin 2 g every 4 to 6 hours.
- Abscesses require drainage.

Secondary Bacterial Cellulitis From Pre-existing Wounds, Trauma, or Skin Lesions

- In eczema and lacerations, infecting organisms are typically *S. aureus* or group A streptococci.
- Cellulitis with an abscess or furuncle, or in postsurgical patients, should prompt antimicrobial coverage including MRSA, pending culture.
- Infected decubitus ulcers are often malodorous and necrotic and are complicated by increasing tenderness and fever. Organisms most commonly present are mixed bowel flora (gram-negative organisms, streptococci, anaerobes).
- Infection of burns is most commonly due to *Pseudomonas aeruginosa,* other gram-negative organisms, *S. aureus,* and *Candida* species.
- Postsurgical cellulitis may be due to gram-negative organisms and can be complicated by wound dehiscence and sepsis. Treat for MRSA, group A streptococci, and gram-negative bacilli.
- Gangrenous cellulitis involves extensive necrosis of subcutaneous tissue and overlying skin and is a rapidly progressive form of cellulitis most commonly caused by group A streptococci. Such streptococcal gangrene most commonly occurs at the site of trauma. Painful erythema is followed by edema, bullae, and necrosis and may be complicated by rapid development of bacteremia and septic shock. Prompt management is critical.
- Infections in diabetic patients with leg ulcers need broader spectrum coverage and are often polymicrobial. Coverage should be for gram-positive, gram-negative, and anaerobic organisms.
- Treat infections from dog and cat bites with oral amoxicillin–clavulanic acid 875 mg/175 mg twice daily for 7 to 10 days. If the patient is allergic to penicillin, use a fluoroquinolone plus clindamycin or trimethoprim–sulfamethoxazole. Cephalosporins are less effective.

Pearls

- Interdigital athlete's foot may be a predisposing condition for cellulitis of the lower extremity. Cultures from the interdigital spaces may yield the pathogenic bacteria.
- Cellulitis is characterized by erythema, edema, and pain. Patients with cellulitis of the leg often have a pre-existing lesion, such

Fig. 6.13 Cellulitis with erythema, edema, and tenderness of the ear.

Fig. 6.14 Sharp demarcation of cellulitis of the arm. The area affected is tender, warm, and swollen. Marking the area is a good way to monitor the expected resolution when receiving treatment.

as an ulcer or erosion, that acts as a portal of entry for the infecting organism.

- Empiric therapy of cellulitis must give good coverage for *S. pyogenes*; if no purulence is present, streptococcal infection is most likely, and trimethoprim–sulfamethoxazole or tetracyclines may not give adequate streptococcal coverage and should not be first choice. In the case of cellulitis with abscess, treat for CA-MRSA.
- Treat aquatic punctures and lacerations for common gram-positive and gram-negative aquatic bacteria (freshwater—a fluoroquinolone; saltwater—doxycycline and ceftazidime or a fluoroquinolone).
- Cellulitis of the pinna may result from infection with *Pseudomonas* species or with staphylococci and streptococci. The lymphatics may be permanently damaged during an attack, predisposing the patient to recurrent episodes of streptococcal erysipelas of the pinna. Recurrent attacks are brought on by manipulation, or even by the slightest trauma.

Pediatric Considerations

- Perianal cellulitis due to group A beta-hemolytic streptococci can be misdiagnosed as candidiasis. Children develop moist, edematous, pink skin around the anus and frequently complain of itch and pain with bowel movements.
- Cellulitis can complicate any cutaneous wound. Some children with varicella are at risk for acquiring invasive forms of group A beta-hemolytic streptococcus (necrotizing fasciitis)—return of fever, tachycardia, and severe skin tenderness are signs that should prompt immediate evaluation for invasive group A streptococcus.
- Necrotizing fasciitis is a complication of group A beta strep infection; the patient may present with flu-like symptoms.

Fig. 6.15 Cellulitis of the leg. There is often a predisposing skin lesion, such as an abrasion, erosion, or fissure, that allows for bacteria to break the skin barrier and gain entry to cause infection.

Fig. 6.17 Perianal cellulitis. Cellulitis (group A beta-hemolytic streptococci) around the anal orifice is often misdiagnosed as candidiasis. It occurs more frequently in children. They are not systemically ill. Culture confirms the diagnosis. Systemic therapy is required.

Fig. 6.16 An early case of cellulitis with diffuse erythema and minimal swelling. Pain was elicited with palpation.

Fig. 6.18 Streptococcal cellulitis occurred under the foreskin simultaneously with anal cellulitis in this adult. Culture is appropriate.

Erysipelas

Description

- Erysipelas is an acute, inflammatory form of cellulitis that differs from other types of cellulitis in that it is superficial, with lymphatic involvement ("streaking") prominent.
- It is more superficial, involving the dermis and upper subcutaneous tissue, and the margins are more clearly demarcated from normal skin than those in classical cellulitis.
- The most common pathogens are group A streptococci. Group B streptococci are noted in infections in the newborn.
- Infection may start at a break in the skin caused by a trauma, a surgical wound, an ulcer or bite, or superficial fungal infection. The site of entry is not always identified.
- More common in infants, young children, and older adults. Risk factors include lymphatic obstruction, postmastectomy, arteriovenous insufficiency, and immunocompromised state.

History

- Onset of the condition is sudden.
- Prodromal symptoms last for 4 to 48 hours and consist of malaise, myalgias, chills, high fever (38°–40° C), and, occasionally, anorexia and vomiting.
- Adenopathy and lymphangitis may also occur.

Skin Findings

- The most common site of involvement is the lower leg. The face, arm, and upper thigh are other common sites. In the neonate, the periumbilical skin is a common site.
- One or more red, tender, and firm spots rapidly increase in size to form a tense and deeply erythematous, hot, sharply demarcated and uniformly elevated shiny patch with an irregular outline and raised border (peau d'orange).
- The color becomes dark and deeply erythematous, and vesicles may appear at the advancing border and over the surface.
- Itching, burning, tenderness, and pain may be moderate or severe.
- Red, sometimes painful, streaks of lymphangitis may extend toward the regional lymph nodes.
- Repeated attacks can impair lymphatic drainage, which predisposes the patient to more infection and permanent swelling. This series of events takes place most commonly in the lower legs of patients with venous stasis and ulceration. Repeated attacks may also occur in the genital skin.

Nonskin Findings

- Predisposing diseases are prior erysipelas, lymphatic or venous circulatory problems, diabetes, renal failure, alcohol abuse, and immunosuppression.

Laboratory

- Streptococci cause 80% of cases; most often the culprits are group A streptococci, followed by group G and other non–group A streptococci. Group G streptococci may be common pathogens, especially in patients older than 50 years.
- *S. aureus, Pneumococcus* species, *Klebsiella pneumoniae, Yersinia enterocolitica,* and *Haemophilus influenzae* are other causative agents.
- The diagnosis is based on the clinical findings; identification of the organism is difficult.
- Only a small percentage of cultures taken from the portal of entry and fluid from intact pustules or bullae are positive. The injection–aspiration method is unreliable.
- Blood cultures are sometimes positive if there is a high fever.

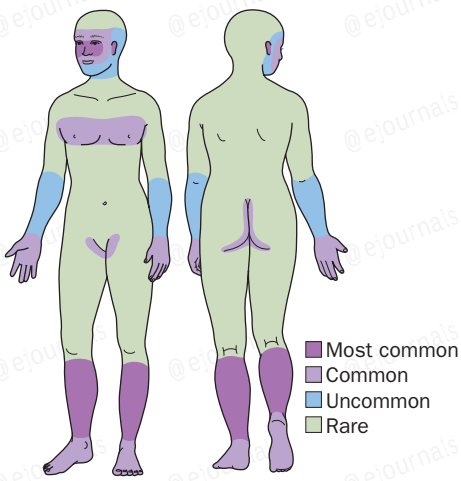

Fig. 6.19 Erysipelas distribution diagram.

- The white blood cell count and erythrocyte sedimentation rate are frequently elevated.

Course and Prognosis

- Recurrences are common in people suffering from local impairment of circulation (e.g., postmastectomy or with chronic venous stasis).
- A relapse may occur in pharyngeal carriers of group A streptococci.
- Poststreptococcal glomerulonephritis is a serious potential complication; streptococcal spread to distant sites is rare but has been reported. Cavernous sinus thrombosis is a serious and rare complication of erysipelas of the face.
- Rare complications include gangrene, sepsis, abscess, and endocarditis.

Discussion

- Erysipelas differs from cellulitis by exhibiting raised, clearly marginated borders and frequent lymphangitic streaking.

Treatment

- In acute episodes, penicillin V orally 250 to 500 mg four times a day for 2 weeks is the drug of choice. Amoxicillin is also effective. Diagnosis of a streptococcal origin should be reconsidered if the response to penicillin is not rapid. Two alternatives for patients who cannot take penicillin are azithromycin (Zithromax) 500 mg on day 1 and 250 mg on day 2 to day 5, and clarithromycin 500 mg every 12 hours for 7 to 14 days.
- Bed rest and elevation of the affected limb are also indicated. Anticoagulant therapy should be considered in people on bed rest who are at risk because of venous thromboembolism.
- Continuous antibiotic prophylaxis is indicated for patients with high recurrence rates. Daily administration of penicillin V orally 250 to 500 mg twice a day, or intramuscularly with benzathine penicillin 1.2 mU every month for 1 year may be of help in prevention of recurrence.

Pearls

- Hospitalization for intravenous antibiotics, rest, and elevation should be considered if there are indications of severe advancing disease, comorbidity, or potential social barriers to appropriate and successful treatment.

Pediatric Considerations

- Children do not often develop erysipelas.
- Erysipelas due to *H. influenzae* rarely occurs because of the introduction of the *Haemophilus* vaccine.

Fig. 6.20 Erysipelas in a patient with diabetes. Note the sharp demarcation of erythema and edema. Erysipelas is usually caused by beta-hemolytic group A streptococcal infection of the superficial dermis.

Fig. 6.21 Erysipelas. Recurrent episodes of infection have resulted in lymphatic obstruction and have caused permanent thickening of the skin.

- Athlete's foot predisposes to erysipelas; it is the most common site for bacterial entry. Treatment of athlete's foot (tinea infection) is important to heal the otherwise compromised skin barrier.
- A common complication of erysipelas is recurrence due to lymphatic damage, subsequent swelling, and lymphedema, which predispose to repeated infection.

Fig. 6.22 Classic acute presentation of erysipelas. The erythema is intense. The patient often develops systemic symptoms of fever, chills, and malaise. Group A streptococcus pyogenes is responsible for most infections. Erysipelas nowadays is most common on the legs.

Fig. 6.23 Intense erythema, sharp demarcation, pain, and vesiculation are present in this patient with erysipelas.

Folliculitis

Description

- *Folliculitis* means an inflammation of the hair follicle, and there are several types.
- Common types include mechanical folliculitis from persistent trauma or tight clothing; another common type is bacterial folliculitis.
- Fungal folliculitis is less common but can result from untreated tinea corporis, or tinea infection in the beard or hair-bearing skin.
- Bacterial folliculitis includes follicular impetigo, a superficial form, and sycosis barbae, a deep form occurring in the beard area.

History

- Usually the eruption is abrupt.
- Bacterial folliculitis can spread by trauma, scratching, or shaving.
- The distribution is variable; often the scalp, arms, legs, axillae, and trunk are involved.

Skin Findings

- Dome-shaped pustules with small erythematous halos arise in the follicle. These lesions are sometimes tender.
- In sycosis barbae, the inflammation is intense and deep; there is marked tenderness.

Laboratory

- Culture is not routinely necessary. *S. aureus* is the most common infecting organism.
- Potassium hydroxide examination of the hair and surrounding scale is performed to exclude an infection by a dermatophyte.

Course and Prognosis

- Most folliculitis responds to antibiotics and hygienic measures. However, bacterial folliculitis may be recurrent if there is a source of bacteria (nasal vestibule in carriers of *S. aureus*).

Discussion

- In a dermatophyte infection (Majocchi's granuloma), hair follicle infection is caused by a dermatophyte fungus. There are inflammatory papules and pustules with surrounding scale and eczematous papules. The results of a potassium hydroxide examination of the hair and surrounding scale are positive.
- In eosinophilic folliculitis, pruritic, extensive follicular papules suddenly appear on the face, neck, and chest. Testing for HIV should be performed. The diagnosis of eosinophilic folliculitis is usually confirmed or suspected by lesional biopsy findings.
- In gram-negative folliculitis, an acneiform eruption suddenly worsens and becomes pustular. Superficial gram-negative bacterial overgrowth occurs in people treated chronically with antibiotics (often for acne).
- In hot tub folliculitis, erythematous papules and pustules appear, primarily on the trunk. *Pseudomonas* species follicular infection is acquired from improperly sanitized hot tubs.
- Mechanical folliculitis results from chronic frictional exposure, such as from wearing tight pants.
- Occlusion folliculitis results from occlusion, such as from exposure to oil, greases, or occlusive ointments.
- *Malessezia* folliculitis often appears on the back and chest. Characteristics are monomorphic pink pustules and papules. The results of potassium hydroxide testing are positive for short hyphae and round spores.
- In steroid folliculitis, multiple monomorphic small pustules and red papules appear within 2 weeks of using systemic corticosteroids; a neutrophilic inflammation of the hair follicles occurs.

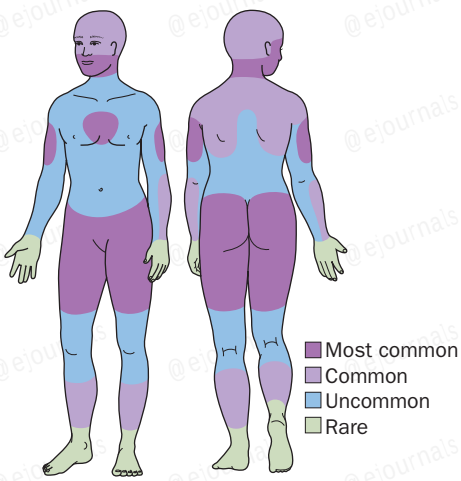

Fig. 6.24 Folliculitis distribution diagram.

Treatment

- Heat, friction, and occlusion should be minimized.
- Antibacterial soap and warm wet dressings are helpful. Razors should be changed frequently to avoid reinfection.
- Mupirocin (Bactroban) applied three times daily for 5 days is effective for limited, superficial involvement. Treat intranasally as well if nasal culture confirms carriage of *S. aureus.*
- Oral antistaphylococcal antibiotics (dicloxacillin, cephalexin) are indicated for extensive or spreading disease or for deep involvement of sycosis barbae, with positive culture for *S. aureus.*
- *Malessezia* folliculitis can be treated with a combination of topical and oral antiyeast antibiotics. Clotrimazole lotion and econazole cream combined with itraconazole 200 mg once a day for 7 days is an effective regimen for widespread *Malessezia* folliculitis. Maintenance ketoconazole shampoo or selenium sulfide shampoo used on affected regions can be helpful.
- Oral antibiotics may need to be discontinued in acne patients with this complication of therapy.
- Follicular dermatophyte infection (Majocchi's granuloma) responds best to oral antifungal therapy. Griseofulvin or terbinafine (Terbinafine 250 mg/day for 4 to 6 weeks) are good therapeutic choices.

Pearls

- Potassium hydroxide examination of the hair and any surrounding scaling should be performed to exclude a dermatophyte infection; failure to consider a dermatophyte infection can result in persistent and sometimes destructive follicular inflammation.
- Staphylococcal folliculitis is the most common form of infectious folliculitis. A group of pustules may appear, usually without fever or other systemic symptoms, on any body surface.
- Nasal carriage of *S. aureus* is a common reason for recurrent bacterial folliculitis. Successful treatment must address the nasal carrier state.

Fig. 6.25 Perifollicular erythema surrounds many follicles. Friction and tight clothing aggravate this problem.

Fig. 6.26 Numerous erythematous macules have developed at the follicular orifices. Staphylococcal folliculitis on the legs can be spread by infected razors and shaving.

Pseudofolliculitis Barbae (Razor Bumps, Ingrown Hairs)

Description

- Pseudofolliculitis barbae is a papular and pustular, foreign body, inflammatory reaction that can affect any individual who has curly hair and who shaves closely on a regular basis.
- This condition is a particular problem in people of Hispanic or African American background.
- It is often chronic and can be disfiguring.

History

- Pseudofolliculitis barbae is a significant problem in predisposed individuals who are required to shave closely.
- It is found in 50% to 75% of African American people and 3% to 5% of white people who shave.
- It is found in both men and women.
- The most severely affected site is the neck area.
- This is a chronic problem unless close shaving is avoided.

Skin Findings

- Pseudofolliculitis barbae affects people with curly hair and those with hair follicles oriented at an oblique angle to the skin surface.
- A sharp, shaved, tapered hair re-enters the skin as it grows from below the skin surface and induces a foreign body reaction, producing a microabscess.
- Perifollicular red papules or pustules appear in the affected skin, most commonly the beard area. The lesions can be both painful and pruritic.
- This condition occurs in any area where the hair is shaved (scalp, posterior neck, groin, legs).
- Scarring and hyperpigmentation may result from this chronic condition.
- Keloid formation is often a problem in affected skin, especially in African American people.

Laboratory

- Typically the lesions are sterile inflammatory papules. The diagnosis is clinical, based on lesion location and appearance.
- Cultured lesions may reveal secondary staphylococcal infection because normal flora may be replaced by pathogenic organisms.

Differential Diagnosis

- Acne
- Folliculitis, bacterial or fungal (culture of a pustule may be helpful, and in resistant, severe, or spreading conditions, a perifollicular scraping or skin biopsy may reveal tinea infection)

Treatment

- The imbedded hair shaft must be dislodged. A needle is inserted under the hair loop, and the hair is firmly elevated.
- A Buf-Puf sponge or toothbrush can be used to gently massage in a circular fashion and thus dislodge any ingrown hair.
- Shaving should be discontinued until inflammation is under control.
- Topical azelaic acid cream (Finacea) will help reduce postinflammatory hyperpigmentation while reducing bacterial colonization.
- Topical antibiotic preparations (clindamycin, benzoyl peroxide 5% or 10%, erythromycin) reduce bacterial colonization and may be beneficial in some patients.
- A short course of antistaphylococcal antibiotics may decrease inflammation and hasten the resolution.
- Intralesional triamcinolone acetonide 2.5 mg/mL is used for persistent papules. Atrophy may result temporarily.
- After lesions resolve, shaving may be resumed.
- Topical eflornithine hydrochloride 13.9% cream (Vaniqa) inhibits ornithine decarboxylase—an enzyme important in hair cell division—and retards hair growth. It is applied twice daily to affected skin. It is well tolerated in most, although a few users develop a mild irritant dermatitis.
- Depilatories (Nair, Neet) with barium sulfide or calcium thioglycolate are effective alternatives to shaving. They are applied to the skin for 3 to 10 minutes and then wiped off. These products are irritating and can be tolerated only once or twice each week.

Fig. 6.27 Folliculitis is inflammation of the hair follicle that is caused by infection, chemical irritation, or physical injury.

- If all measures fail, shaving must be discontinued indefinitely.
- The only cure is permanent removal of the hair follicle. Laser-assisted hair removal may provide a safe, effective means of treating recalcitrant cases. Laser hair removal can be performed with the diode laser (800–810 nm), pulsed alexandrite (755 nm), Nd-YAG (1064 nm), and pulsed noncoherent light source. Adverse effects include pigmentary alteration, including postinflammatory hypopigmentation in people with dark skin, because melanin is the target of laser hair removal.

Shaving Instructions

- The goal is to avoid close shaves and the production of sharply angled hair tips.
- The patient should hydrate the beard before shaving. Shower before shaving and keep the beard hair in contact with warm water for at least 2 minutes.

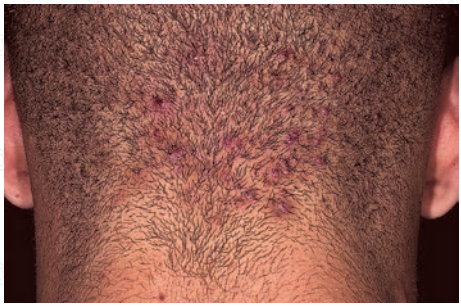

Fig. 6.28 Acne keloidalis is an eruption that appears on the back of the neck. It is most often found in African American men.

- Dislodge any hair tips that are beginning to pierce the skin. A soft-bristled toothbrush in a circular motion or a needle cleaned with rubbing alcohol should be used. This is done before shaving and at bedtime.
- Use thick-lathering shaving gels (e.g., Aveeno Therapeutic Shave Gel, Edge Gel for Tough Beards).
- The Bump Fighter disposable razor (http://www.asrco.com) cuts the hair slightly above the skin surface.
- Alternatively, an electric razor can be used, but avoid the "closest" shave setting.
- The patient should shave in the direction of hair growth. The skin should not be stretched.
- Multiple razor strokes should be avoided.
- A moisturizing lotion should be used after shaving. LactiCare-HC (1% or 2.5%) can be used intermittently to reduce inflammation.

Pearls

- Pseudofolliculitis is a foreign body reaction to hair. The problem is more severe in the neck area, where hair follicles are more likely to be oriented at low angles relative to the skin surface, making repenetration of the skin more likely.
- The avoidance of close shaving is recommended.
- Presently, laser hair removal appears to offer the best long-term results in this otherwise chronic condition.

Fig. 6.29 Pseudofolliculitis is a foreign body reaction to hair. The disease occurs only in men who have commenced shaving. It begins with the appearance of small follicular papules or pustules and rapidly becomes more diffuse as shaving continues.

Fig. 6.30 Pseudofolliculitis. The problem is more severe in the neck area, where hair follicles are more likely to be oriented at low angles to the skin surface, making repenetration of the skin more likely.

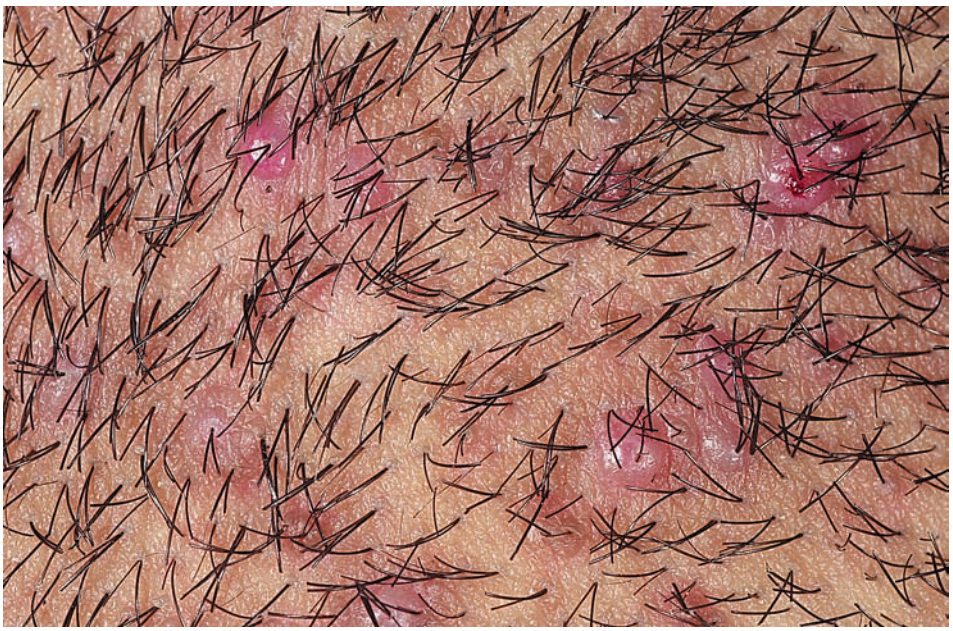

Fig. 6.31 Acne keloidalis presents as hard papules with hair emerging from the center. Laser hair removal may play a role in early prevention, but its use is limited in darker skin types. The 810 diode and 1064 nm NdYag laser are options. Intralesional steroid injections are often a typical first line treatment.

Furuncles and Carbuncles

Description

- A furuncle (boil) is a walled-off, deep and painful, firm or fluctuant mass enclosing a collection of pus; often, it evolves from a superficial folliculitis.
- *S. aureus* is the most commonly associated organism, but other organisms (*Escherichia coli, P. aeruginosa, Streptococcus faecalis*) and anaerobes (*Peptostreptococcus, Peptococcus,* and *Lactobacillus* species) may cause lesions.
- Usually, a bacteriologic study of the abscess identifies the local flora.
- A carbuncle is an extremely painful, deep, interconnected aggregate of infected, abscessed follicles.

History

- Furuncles and carbuncles are uncommon in children.
- Occlusion and hyperhidrosis promote bacterial colonization.
- Most affected patients have normal immune systems, although certain conditions and immune defects may predispose the patient to furuncles and carbuncles (e.g., hyperimmunoglobulin E syndrome, chronic granulomatous disease, Wiskott–Aldrich syndrome, Chédiak–Higashi syndrome, diabetes, leukemia, therapeutic immunosuppression, malnutrition, obesity).
- Whirlpool baths at nail salons are a risk for mycobacterial furunculosis.

Skin Findings

- Any hair-bearing site can be affected. Sites of high friction and sweating are most typically affected; these include the areas under the belt, the anterior thighs, the buttocks, the groin, the axillae, and the waist.
- With a furuncle, a deep dermal or subcutaneous, red, swollen, and painful mass later points toward the surface and drains through multiple openings.
- With a carbuncle, deep, tender, firm subcutaneous erythematous papules enlarge to deep-seated nodules that can be stable or become fluctuant within several days.
- Favored sites for carbuncles are the back of the neck, the upper back, and the lateral thighs.

Nonskin Findings

- With a furuncle, the patient remains afebrile.
- With a carbuncle, malaise, chills, and fever may precede or occur during the height of inflammation.

Laboratory

- Gram stain, culture, and sensitivity are indicated and will help guide appropriate antibiotic therapy.

Differential Diagnosis

- Ruptured pilar or epidermal cyst
- Cystic acne
- Hidradenitis suppurativa
- Early lesion of pyoderma gangrenosum
- Infected or ruptured molluscum contagiosum

Course and Prognosis

- The abscess either remains deep and is reabsorbed or points toward the surface and ruptures.
- A ruptured lesion heals with a depressed, violaceous scar.
- Infection can spread to other sites.
- Recurrent furunculosis can be difficult to eradicate.

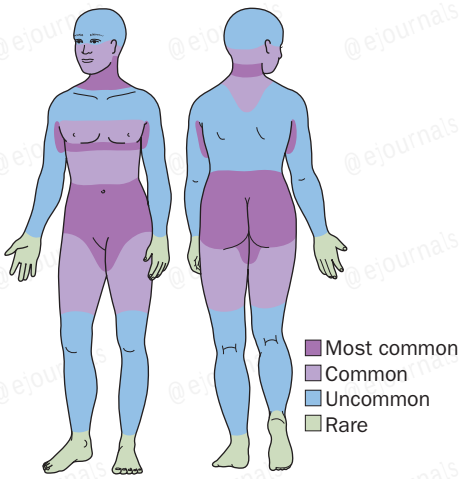

Fig. 6.32 Furuncles and carbuncles distribution diagram.

Treatment

Furuncles and Carbuncles

- Warm, moist dressings are applied to the lesion 15 to 30 minutes several times a day. A culture and sensitivity test is often appropriate.
- Incision and drainage are the primary management for pointing, fluctuant lesions.
- Periodic follow-up and re-evaluation are recommended to ensure wound improvement and treatment response.
- Systemic antibiotic therapy is indicated for patients with multiple lesions or signs of systemic illness (fever, malaise, spreading redness, increasing discomfort).
- The incidence of MRSA is increasing, making culture and sensitivity data increasingly important.
- Dicloxacillin 500 mg four times daily for 10 days or cephalexin 500 mg four times daily for 10 days is used in adults with MRSA.
- Clindamycin 150 to 300 mg four times daily for 10 days is used in adults, and re-evaluation and hospitalization for intravenous antibiotic therapy should be considered.

Recurrent Furuncles and Carbuncles

- This is most commonly caused by MRSA. CA-MRSA is becoming endemic. Good hand-washing technique with soap and water will reduce the number of bacteria on the skin. The affected person should use separate towels for drying.
- Methicillin-resistant carrier state can be treated with to mupiricin 2% into the nose or one wounds twice daily for 5 days. If other measures fail, one trimethoprim–sulfamethoxazole double-strength tablet is given twice daily orally for 10 days.
- Maintenance regimens with mupirocin may induce resistance in roughly 10% of patients.
- Other measures include washing the entire body and fingernails each day for 1 to 3 weeks with Betadine and changing and hot-cycle washing the towels, washcloths, bed sheets, and underclothing daily. The patient should change the wound dressings frequently, clean or replace shaving tools daily, and avoid nose picking. Bathing with chlorhexidine solution 4% as a wash or dilute bleach baths (¼ cup regular bleach in a half tub of water, soak for 5–10 minutes

Fig. 6.33 Round, deep, tender nodules on the legs in this patient with staphylococcal furunculosis. Recurrent bouts of this problem require careful, multistep management.

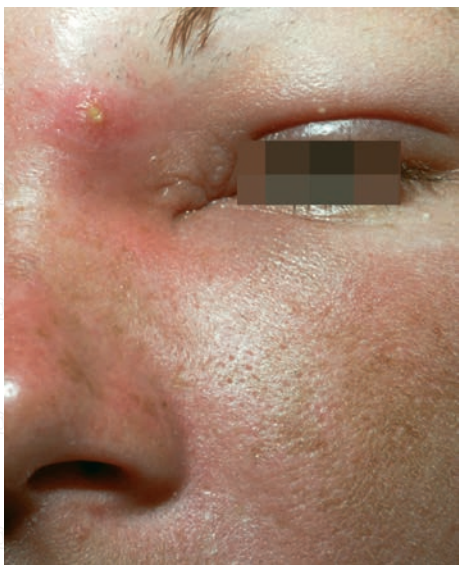

Fig. 6.34 A furuncle in the left upper inner canthus. Systemic antibiotics are indicated to prevent further spread of the infection.

two to three times a week) can reduce skin colonization.
- Applicable predisposing factors must be addressed, including friction, tight clothing, exposure to industrial chemicals, obesity, poor hygiene, and diabetes.

Pearls

- The primary management for a solitary furuncle is incision and drainage.
- Secondary dissemination due to bacteremia can occur and is a greater risk in people who are immunocompromised and in those with alcoholism or diabetes. Seeding of artificial valves, grafts, long bones, kidneys, or joints is a risk.
- The nasal carriage of *S. aureus* and carriage of the bacterium in the folds or perineum should be evaluated by culture in cases of chronic recurrent furunculosis.

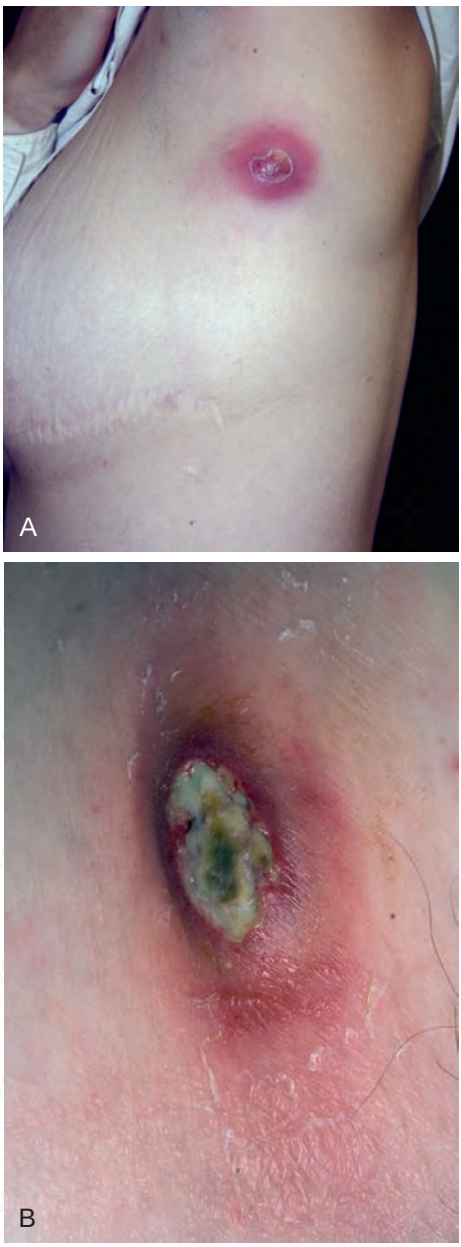

Fig. 6.35 A furuncle is an abscess that exudes purulent material from a single opening. Treatment involves draining the lesion, culture, and systemic antibiotics.

Fig. 6.36 A furuncle has rapidly evolved in a plaque of atopic dermatitis. The center is swollen and soft and will soon rupture and exude purulent material.

Fig. 6.37 Furuncles and carbuncles. The abscess either remains deep and reabsorbs, or points and ruptures through the surface. This lesion ruptured and formed a crust. Oral antibiotics were not required, and the lesion resolved without treatment.

Pseudomonas Folliculitis

Description

- *Pseudomonas* folliculitis is an acute skin infection that follows exposure to contaminated water.
- Multiple urticarial red plaques with a central papule or pustule are highly distinctive typical lesions.
- This is also called *hot tub folliculitis*.

History

- The attack rate is significantly higher in children than in adults, possibly because children tend to spend more time in the water.
- *Pseudomonas* folliculitis occurs 8 hours to 5 days (or longer) after using a contaminated pool (whirlpool, hot tub, physiotherapy pool) or water slide, or a contaminated loofah sponge.
- The attack rate is variable; 7% to 100% of those exposed to *Pseudomonas* species develop the disease.
- The spread of infection from person to person is unlikely.
- Prolonged exposure to the water, excessive numbers of bathers, and inadequate pool care predispose to infection.
- Desquamated skin cells in the water provide a rich, organic nutrient source for bacteria.
- In most cases, the eruption clears in 7 to 10 days without any treatment, but recurrent crops of lesions may occur for as long as 3 months.

Skin Findings

- Plaques are 0.5 to 3 cm and are red, pruritic, round, and urticarial with a central papule or pustule.
- A few plaques to more than 50 occur primarily on the trunk.
- The rash may be a follicular, maculopapular, vesicular, pustular, or polymorphous eruption that includes all of these types of lesions.
- The rash is most severe in areas occluded by snug bathing suits.
- Occlusion and superhydration of the stratum corneum favors colonization of the skin with *P. aeruginosa.*
- Women who wear one-piece bathing suits are at an increased risk.
- The rash resolves, leaving round spots of red to brown, postinflammatory hyperpigmentation.

Nonskin Findings

- Fever, malaise, and fatigue may occur during the initial few days of the eruption, but this is uncommon.

Laboratory

- *P. aeruginosa* serotypes 0:9 and 0:11 are most commonly isolated from skin lesions, but other serotypes have been reported.

Differential Diagnosis

- Staphylococcal folliculitis
- Hives
- Insect bites

Treatment

- The infection is self-limited and usually resolves in 5 days; treatment is usually not required.
- A wet dressing of acetic acid 5% (white vinegar) is applied for 20 minutes twice or four times a day. Silver sulfadiazine cream (Silvadene) can help.
- Severe cases or cases resistant to topical therapy can be treated orally with ciprofloxacin 500 mg twice daily for 5 to 10 days.

Preventative Measures

- Continuous water filtration eliminates desquamated skin.
- Adequate chlorine levels should be maintained.
- The water in private hot tubs should be changed every 4 to 8 weeks.
- Public hot tubs should be drained daily.
- Showering after using the contaminated facility offers no protection.

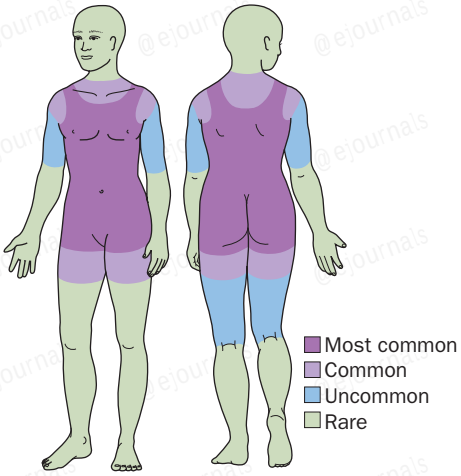

Fig. 6.38 *Pseudomonas* folliculitis distribution diagram.

Fig. 6.39 Bright-red edematous papules with central pustules are scattered on the buttocks in this patient with *Pseudomonas* folliculitis. The lesions are typically on the trunk in areas of skin covered by the bathing suit.

Fig. 6.40 The lesions start as itchy macules and progress to pustules. An infected hot tub is to blame.

Fig. 6.41 *Pseudomonas* folliculitis. The rash may be a follicular, maculopapular, vesicular, pustular, or polymorphous eruption that includes all of these types of lesions.

Otitis Externa

Description

- Otitis externa is an inflammation of the external auditory canal, usually with secondary infection.

History

- Otitis externa is found equally among males and females.
- A mild self-limited form known as *swimmer's ear* is especially common in children, often in the summer.
- No racial or genetic predisposition has been reported.
- Symptoms range from itch and irritation to severe pain.
- Mechanical cleansing of the external canal and medicaments used to relieve symptoms can mask or exacerbate the condition.
- Cerumen is produced by modified apocrine glands of the external auditory canal. It forms a water-resistant barrier for the thin skin that lines the canal. It inhibits bacterial growth by maintaining a low pH environment. When this protective barrier is disrupted, bacterial overgrowth can occur.
- The usual pathogen is *Pseudomonas* species, but mixed infections with *Staphylococcus* and *Pseudomonas* species are common.
- Swimmer's ear is typically caused by *Pseudomonas*, *Enterobacteriaceae,* or *Proteus* species. Acute infection is usually due to *S. aureus.*
- Secondary infections with *Candida* species may also occur but are uncommon.

Skin Findings

- Dull pain is localized to the external auditory canal.
- The external auditory canal is inflamed with erythema and edema.
- Keratin and inflammatory cell debris accumulate within the canal. Most cases do not progress beyond this point.
- With progression, the pinna becomes red, hot, and edematous.
- Cellulitis involves the entire pinna and often extends to the preauricular skin. At this point, pain becomes sharp and constant.
- Purulent drainage exudes from the external auditory canal.

Nonskin Findings

- The regional lymph nodes are usually palpable and tender.

Laboratory

- A skin biopsy is not recommended.
- The external auditory canal should be cultured.

Course and Prognosis

- The protective barrier of cerumen may be compromised by any number of mechanisms.
- Mechanical disruption (i.e., vigorous cleansing of the canal), inflammatory conditions (e.g., psoriasis, seborrheic dermatitis), and contact dermatitis (irritant and allergic) may all lead to disruption of the barrier.
- A rare and severe form of otitis, referred to as *malignant external otitis,* may develop in patients who have diabetes or who have had ear surgery. Cellulitis extends from the external auditory canal into the bone at the

Fig. 6.42 *Pseudomonas* cellulitis. The entire pinna and surrounding skin have become inflamed after an episode of external otitis.

base of the skull. The ipsilateral facial nerve becomes involved.

- Lymphatic drainage from the pinna may be altered by cellulitis. Such patients may be predisposed to future episodes of streptococcal erysipelas of the pinna.

Discussion

- Early in the course, the differential diagnosis includes psoriasis, seborrheic dermatitis, and contact dermatitis. Any of these conditions can lead to compromise of the natural barrier and ultimately to otitis externa.
- Herpes zoster infection involving the geniculate ganglion and Ramsay–Hunt syndrome can mimic early otitis externa with localized pain and inflammation. Careful examination reveals vesicles within the external auditory canal. Usually, an

Fig. 6.44 Otitis externa. Erythema begins in the ear canal. Traction on the ear produces pain. The canal usually contains moist debris. Eczema of the pinna, as occurs in this case, may be present.

Fig. 6.43 Malignant external otitis. Patients have a history of nonresolving otitis externa of many weeks' duration. Most patients have diabetes. *Pseudomonas* organisms invade underlying soft tissues. There is severe ear pain, a purulent exudate, and granulation tissue. Nuclear scanning studies and computed tomography scans may reveal osteomyelitis of the skull base.

Fig. 6.45 Culture of the skin is indicated to ensure proper treatment of this edematous, inflamed pinna.

ipsilateral Bell's palsy is present, or it develops soon after onset.
- When cellulitis involves the ear, the differential diagnosis includes relapsing polychondritis, a recurrent phenomenon presumably of autoimmune origin. Purulent discharge is not seen in this condition.

Treatment

- Treatment involves re-establishing the natural protective barrier.
- Cellular debris is flushed from the external canal with gentle irrigation.
- An acetic acid solution (VoSol otic solution or VoSol HC otic solution) helps lower the pH and inhibits bacterial and fungal growth.
- Ofloxacin otic solution 0.3% (Floxin otic solution twice daily) or ciprofloxacin and hydrocortisone (Cipro HC otic) are instilled twice a day. For acute disease, oral dicloxacillin 500 mg four times daily is prescribed.
- Topical steroids, wet dressings using an astringent (e.g., Domeboro), or Bluboro wet dressings applied for half an hour three times daily and oral antibiotics, such as ciprofloxacin (Cipro), are of value when cellulitis involves the pinna.
- Avoidance of the more common contact allergens (e.g., topical bacitracin, neomycin, and hydrocortisone) and review of other topical product contents for possible contact allergens can minimize the chance of a contact allergy complicating this problem.
- Vigorous scratching, rubbing, or mechanical débridement of the external auditory canal can remove protective wax defenses and should be strongly discouraged.
- Malignant external otitis requires hospitalization, the administration of intravenous antibiotics, and débridement, as well as consideration of a computed tomographic scan or magnetic resonance imaging scan to evaluate possible osteomyelitis.
- An otolaryngology consultation is recommended.

Pearls

- Chronic otitis externa is often secondary to an underlying skin condition, such as seborrhea, psoriasis, or contact allergy. Seborrhea should be controlled with an antidandruff shampoo, such as selenium 2.5% or ketoconazole shampoo, and a medium-potency steroid solution, such as fluocinolone acetonide solution 0.01% twice daily. Consider patch testing for contact allergy that aggravates this problem.
- In malignant otitis externa there is typically a history of nonresolving otitis externa of many weeks' duration. Most patients have diabetes. *Pseudomonas* species organisms invade underlying soft tissues. There is severe ear pain, purulent exudate, and granulation tissue.

Table 6.1 Antibiotics

Generic Name	Tablets/Capsules (mg)	Liquid (mg/mL)
Penicillins		
Amoxicillin	125,* 250,* 400,* 250, 500, 875, 1000, 3000	50/1, 125/5, 250/5, 400/5, 500/5
Amoxicillin–clavulanate	125, 125,* 200,* 250,* 375, 400,* 250, 500, 875, 1000†	125/5, 200/5, 250/5, 400/5
Ampicillin	125,* 250, 500, 1000	100/1, 125/1.25, 125/5, 250/5, 500/5
Dicloxacillin	125, 250, 500	62.5/5
Nafcillin	250, 500	250/5
Oxacillin	250, 500	250/5
Penicillin V potassium	125,* 250, 300, 312.5, 500, 625, 937.5	125/5, 180/5, 250/5, 300/5
Cephalosporins		
First Generation		
Cefadroxil	250, 500, 1000	125/5, 250/5, 500/5, 500/10
Cephalexin	250, 500, 1000	100/1, 125/1.25, 125/5, 250/5, 375/5, 500/5
Cephradine	250, 500, 1000	125/5, 250/5
Second Generation		
Cefaclor	250, 375,§ 500, 500§	125/5, 187/5, 250/5, 375/5
Cefprozil	250, 500	125/5, 250/5
Cefuroxime	125, 250, 500	125/5, 250/5
Tetracyclines		
Doxycycline	20, 50, 100, 100§, 150§	25/5, 50/5
Minocycline	50, 75, 100	50/5
Tetracycline	50, 100, 250, 500	125/5
Macrolides, Others		
Azithromycin	250, 500, 600, 1000	100/5, 200/5, 2000/60§
Clarithromycin	250, 500, 500§	125/5, 125/15, 187.5/5, 250/5
Erythromycin base	250, 250,§ 333, 333,§ 500, 500§	
Erythromycin stearate	100, 250, 500	100/2.5, 125/5, 200/5, 250/5
Erythromycin ethylsuccinate	200,* 400, 600	100/2.5, 125/5, 200/5, 400/5
Erythromycin estolate	125, 125,* 250, * 250, 500	100/1, 125/1, 125/5, 250/1, 250/5
Clindamycin	75, 150, 300	75/5

*Chewable.
†Extended release.
§Sustained release.

Sexually Transmitted Infections

7

M. Shane Chapman

Syphilis

Description

- Syphilis is a sexually transmitted infectious disease caused by the spirochete *Treponema pallidum.*
- The infection can affect any organ and may mimic various other diseases; thus it has been called the "great imitator."
- If left untreated syphilis can infect and damage the heart, aorta, brain, eyes, and bones and can be fatal.
- Syphilis passes through three distinct stages: primary infectious, secondary and latent, or progression to a rare tertiary stage.

History

- Syphilis was named after an afflicted sheep herder named Syphilus in a 1530 poem by Girolamo Fracastoro.
- In the past, syphilis was called the *French disease* but was also known as the *Christian disease*, the *Great Pox, Cupid's disease,* and the *Black Lion*; it was most well-known as *lues, lues venereal,* or *venereal plague*.
- It is believed the disease was introduced to Europe by Columbus after returning from the West Indies, and its spread within Europe was blamed on the frequent wars within the region at that time.
- Incidence declined after World War II because of effective penicillin treatment.
- The Tuskegee study in 1932 is a dark part of medical and syphilis history, in which penicillin therapy for black men who were infected with syphilis was withheld in order to study the short-term and long-term effects of the disease.
- Syphilis has become more common since the 1980s with the introduction of AIDS.

Primary Syphilis

- Initially, syphilis appears as a cutaneous ulcer or chancre after direct contact with another infectious lesion.
- The chancre appears 10 to 90 days (average, 21 days) after exposure.
- Chancres are usually solitary, but multiple lesions can occur.
- Untreated primary chancres resolve in 75% of cases, but the spirochete remains within the host.

Secondary Syphilis

- Secondary syphilis results from hematogenous and lymphatic spread of the spirochete.
- The secondary stage begins approximately 6 weeks after the chancre appears and lasts for 2 to 10 weeks.
- An influenza-like syndrome occurs with mucocutaneous lesions, hepatosplenomegaly, and generalized adenopathy.
- The distribution and morphologic characteristics of individual skin lesions vary.
- Secondary syphilis lesions most commonly manifest as pink, scaly 1- to 2-cm patches that become generalized. This eruption closely resembles pityriasis rosea.
- This stage of syphilis is contagious and can be spread by touch.
- Syphilis in this stage is easily confused with numerous other cutaneous and systemic diseases, and therefore it has been termed the "great imitator."
- In addition to the previous cutaneous findings, secondary syphilis may manifest as fever, pharyngitis, weight loss, headache, meningitis, hepatitis, renal disease, gastritis, colitis, arthritis, keratitis, and uveitis.

Latent Syphilis

- Latent syphilis is a state of positive serologic tests (not false positive) without evidence of active disease.
- It has an early status and a late status.
- The early latent period begins 2 years or less from the onset of primary disease, without signs or symptoms of disease.

- Late latent syphilis is infection with the spirochete for longer than 2 years, without clinical evidence of disease.
- Early latent syphilis can be treated with one intramuscular injection of long-acting penicillin.
- Late latent syphilis requires 3 weekly injections, but is not as "infectious" as early latent syphilis.

Fig. 7.1 Primary syphilis: the originating papule of syphilis becomes necrotic and ulcerates into a shallow 3 mm, usually painless ulcer, that eventually becomes indurated with a white to yellow serous exudate at the bottom of the ulcer.

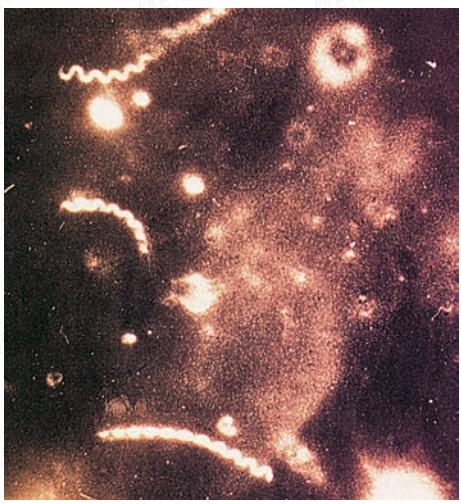

Fig. 7.2 Darkfield microscopy shows the spirochete, *Treponema pallidum,* which is the infective organism that causes syphilis. Routine culture is not sufficient to identify the spirochete.

Fig. 7.3 Primary syphilis. The borders of the ulcer are raised, smooth, and sharply defined.

- Half of patients with early latent syphilis will progress to late-stage syphilis.

Tertiary Syphilis

- Tertiary syphilis is characterized by a small number of organisms eliciting a large or brisk cellular immune response, with many clinical manifestations.
- Systemic disease develops in about 25% of untreated or inadequately treated cases.
- Tertiary syphilis typically develops 1 to 10 years after initial infection.
- Cardiovascular and central nervous system involvement, with systemic granulomas or gummas, are the hallmarks of this stage.

Congenital Syphilis

- *T. pallidum* can be transmitted from an infected mother to her fetus.
- In untreated cases, 25% of neonates are stillborn, 25% die shortly after birth, 10% have no symptoms, and 40% will have late symptomatic congenital syphilis.
- In early congenital syphilis, rash, hepatosplenomegaly, and bone and joint changes occur before age 2 years.
- In late congenital syphilis, bone and joint changes, neural deafness, and interstitial keratitis occur after age 5 years.
- Therapy before the 16th week of gestation usually prevents infection of the fetus.
- A fetus is at greatest risk when the mother has syphilis for less than 2 years.

Skin Findings

Primary Syphilis

- The chancre begins as a papule or nodule, then undergoes ischemic necrosis and erodes and ulcerates.
- The chancre is usually 3 mm to 2 cm, with a firm, raised, sharply defined border.
- These lesions may be asymptomatic and undetected on the cervix of women, allowing transmission to the unsuspecting.
- Painless, hard, discrete, nonsuppurative regional lymphadenopathy develops in 1 to 2 weeks.
- The chancre heals with scarring, typically in 3 to 6 weeks.

Secondary Syphilis

- This stage of syphilis is characterized by systemic, cutaneous, and mucosal signs and symptoms.
- Fever, malaise, pharyngitis, adenopathy, weight loss, and meningeal signs (headache) are common.
- The most common sign is a nonpruritic generalized, pink, scaly papular eruption (80%).
- The patches develop slowly; appear in a variety of shapes, including round, ellipsoid, oval, or annular; and persist for weeks or months.
- Symmetric hyperpigmented oval papules with a collarette of scale appear on the palms or the soles in most patients.
- Irregular alopecia of the beard, scalp, and eyelashes occurs, which is sometimes referred to as *moth-eaten alopecia*.
- Whitish, moist, anal condyloma lata lesions are highly infectious wart-like papules that are characteristic of syphilis and may be confused with condyloma accuminata (warts).
- Split papules appear at the angle or commissures of the mouth.
- All secondary lesions are highly infectious with direct contact or palpation.
- Without treatment, lesions of this stage relapse in about 20% of patients within a year.

Latent Syphilis

- There are very few if any clinical signs of syphilis in this stage.

Fig. 7.4 Secondary syphilis. Oval-shaped keratotic macules have slight hyperpigmenation characteristic of syphilis.

Fig. 7.5 Secondary syphilis. Small annular patches with slight scale spread diffusely over the trunk, mimicking eczema and psoriasis.

Tertiary Syphilis

- Cutaneous gummas or granulomatous nodules develop subcutaneously, expand, and ulcerate.
- These lesions also occur in the liver, bones, and other organs.
- Gummas produce a chronic inflammatory state in the body and produce distortion and malfunction with mass effects.

Fig. 7.6 Secondary syphilis. Patchy "moth-eaten" alopecia of the scalp, beard, and eyelashes may occur in secondary syphilis and resembles tinea capitis.

Fig. 7.7 Secondary syphilis. Small, white, shiny papules consistent with cutaneous lesions seen in syphilis.

- Untreated tertiary syphilis can also cause neuropathic joint disease and degeneration of bones.
- Cardiovascular syphilis includes syphilitic aortitis, aortic aneurysm, and cardiac valve problems.
- Neurosyphilis can manifest as a generalized paresis, personality and emotional changes, and hyperactive reflexes.
- Infection and inflammation of the spinal cord can cause the characteristic shuffling gait of syphilis or tabes dorsalis.

Laboratory and Testing

- Direct detection of the treponemal spirochete is diagnostic.
- Detection of the spirochete from skin lesions can be achieved under darkfield microscopy, which shows corkscrew rotation motility of the small, spiral syphilis spirochete, but must not be confused with other spirochete infections.
- There are two quick and inexpensive serologic screening tests: the rapid plasma reagin (RPR) test and the Venereal Disease Research Laboratory (VDRL) test.
- These screening tests are reactive by day 7 of the chancre and are easy to perform but may have false-positive results from other viral infections, tuberculosis, malaria, and some connective tissue diseases.
- Some laboratories are screening samples using treponemal tests, typically by enzyme-linked immunosorbent assay (ELISA) or chemiluminescence immunoassay. This reverse screening algorithm for syphilis testing can identify persons previously treated for syphilis, those with untreated or incompletely treated syphilis, and those with false-positive results that can occur with a low likelihood of infection.
- Latent syphilis can be diagnosed by these reactive screening tests.
- Because of the possibility of false-positive results from the RPR and VDRL tests, positive results from the screening tests should be confirmed with a fluorescent treponemal antibody, absorbed test (FTA-ABS) or the *T. pallidum* hemagglutination assay (TPHA), which are more specific but more expensive.
- The FTA-ABS and TPHA tests are also positive for pinta and yaws, so clinical correlation is required.
- One third of latent syphilis-infected people have a negative or nonreactive result on the RPR test. They show no signs of disease and only have a positive result on the microhemagglutination *T. pallidum* antibody test. Another one third have a positive RPR test and microhemagglutination *T. pallidum* test, and the remaining one third have clinical symptoms of tertiary disease.
- Tertiary syphilis is diagnosed by elevated cerebrospinal fluid pressure, protein concentration, and specific antitreponemal antibodies in the cerebrospinal fluid.
- False-positive results are possible with all of these serologic tests.
- Neurosyphilis is confirmed by high numbers of leukocytes in the cerebrospinal fluid or high protein concentration.
- VDRL or FTA-ABS of the cerebrospinal fluid is also usually performed to diagnose neurosyphilis.

Differential Diagnosis

Primary Syphilis

- Herpes simplex
- Chancroid
- Behçet syndrome
- Fixed drug eruption
- Traumatic ulcers

Secondary Syphilis

- Pityriasis rosea
- Guttate psoriasis
- Lichen planus
- Tinea versicolor
- Exanthematous drug eruption
- Viral eruptions

Treatment

- In early disease (primary, secondary, latent less than 1 year), the drug of choice is benzathine penicillin G 2.4 million units intramuscularly, given once.
- In late disease (lasting more than 1 year), the drug of choice is benzathine penicillin G 2.4 million units intramuscularly once a week for 3 weeks consecutively.
- People who are allergic to penicillin and not pregnant can be given doxycycline 100 mg twice a day for 2 weeks, or tetracycline 500 mg four times a day for 2 weeks. See http://www.cdc.gov/std/treatment/ for other alternatives.
- Successful therapy is indicated by a falling RPR titer.
- RPR testing should be repeated 3, 6, and 12 months after treatment is complete.
- Treatment is repeated when there is a sustained fourfold increase in the RPR titer.
- Therapy is repeated when a high titer does not show a fourfold decrease within 1 year.
- In most patients infected with HIV, syphilis responds to standard treatment regimens.

Fig. 7.8 Secondary syphilis. Diffuse pink asymptomatic patches with polymorphic shapes and sizes are characteristic of secondary syphilis.

Fig. 7.9 Secondary syphilis. Early in the secondary stage of syphilis, sparsely scattered pink to oval-shaped patches resemble pityriasis rosea, which may result in misdiagnosis.

Fig. 7.10 Secondary syphilis. Lesions on the palms and soles occur in most patients with secondary syphilis. A brown coppery color is characteristic of secondary syphilis.

Pediatric Considerations

- Congenital syphilis (early and late) is acquired from an untreated or inadequately treated pregnant woman.
- Early adequate treatment of the mother can prevent severe birth defects.
- Early congenital syphilis appears in the perinatal period (up to 2 years of age) but typically manifests in the first 3 months of life.
- Children develop the following main symptoms:
  - Skin: scaling of palms and soles (51%), papulosquamous eruption (44%), eroded intertriginous papules (17%), periorificial rhagades (14%)
  - Bone: osteochondritis periostosis (80%)
  - Pain with handling (38%)
  - Nasal congestion (snuffles) (18%)
  - Hepatosplenomegaly (48%)
- Late congenital syphilis begins at age 2 with the following manifestations:
  - Frontal bossing (81%)
  - Underdeveloped maxillae (83%)
  - High-arched palate (76%)
  - Saddle nose (73%)
  - Dome-shaped molars with multiple poorly formed molars (65%) and notched incisors, or Hutchinson's teeth (63%)
  - Proximal clavicular thickening (39%)
  - Interstitial keratitis (9%)
  - Saber shins (4%)
  - Deafness (3%)
- All patients with syphilis should be tested for HIV.

Chancroid

Description

- Chancroid is a rare sexually transmitted disease caused by the gram-negative streptobacillus, *Haemophilus ducreyi.*
- It is characterized by painful genital ulceration and inguinal lymphadenopathy.
- The infection is also known as *soft chancre* and *ulcus molle*.

History

- It is more common in heterosexual men, who obtain it from asymptomatic carriers, usually prostitutes; the male-to-female ratio is 10:1.
- It is more common in developing countries and in people who travel to those countries but is rare in the United States.
- The ulcer from chancroid is a risk factor for coinfection with HIV.

Skin Findings

- Chancroid has an incubation period from 1 day to 2 weeks from the time of initial infection.
- Most lesions occur on the genitalia, especially the coronal sulcus of the penis in men and fourchette and labia minora in women, but also occur on the thighs, buttocks, and perianal area.
- Half of men have a single ulcerative lesion, whereas women are more likely to have multiple lesions, but less pain.
- A painful red papule first appears at the site of inoculation within 1 or 2 days, followed by a pustule, which may rupture, forming an ulcer with a bright red base.
- The ulcer of chancroid is deep, bleeds easily, is covered by a yellow to gray fibrinous exudate, and may spread laterally.
- The ulcer sizes vary from 3 mm to 5 cm in diameter.
- Women are more likely to develop "kissing ulcers" or bilateral ulcers on opposing surfaces of the labia and perineal area.
- These ulcers are highly infectious and may become multiple through autoinoculation.

Nonskin Findings

- Patients may feel ill, with fever, anorexia, and malaise.
- Unilateral or bilateral inguinal suppurative lymphadenopathy develops in 50% about 1 week after infection.
- Lymph nodes may suppurate and ulcerate or resolve spontaneously.
- Women may carry the organism, but may not display any clinically detectable lesions and have no symptoms.
- Women, more than men, may also present with dysuria or dyspareunia.
- Untreated cases either resolve spontaneously or become chronic and require a long time to heal.

Laboratory

- *H. ducreyi* cannot be cultured on routine media.
- Newly formulated transport media can maintain the viability of the organism.
- A cotton swab is used to obtain a specimen at the base of the ulcer, which is then rolled over a glass slide. Gram-negative clumped organisms, resembling a "school of fish," can be seen and are diagnostic.
- There is a high rate of coinfection with HIV among patients with chancroid, so a test for this virus is reasonable in these patients. Syphilis serologies should also be considered.

Differential Diagnosis

- Herpes simplex
- Syphilis
- Lymphogranuloma venereum
- Granuloma inguinale
- Traumatic ulceration

Treatment

- Azithromycin 1 g orally in a single dose.
- Ceftriaxone 250 mg intramuscularly in a single dose.
- Ciprofloxacin 500 g orally twice daily for 3 days.
- Erythromycin base 500 mg orally four times daily for 7 days.

Pearls

- Herpes simplex is the most common form of genital ulceration in North America, but this typically presents as small grouped papules and vesicles, not large ulcers.

- The combination of painful genital ulceration and ulcerative and/or suppurative inguinal adenopathy is highly suggestive of a diagnosis of chancroid in high-risk geographic areas.
- Syphilis can also present as a single ulcer or chancre, but may be less painful than chancroid and considered a "hard ulcer."
- Chancroid infection is strongly associated with coinfection with HIV.
- Treatment of chancroid should not be delayed for culture results if the disease is suspected. Prolonged genital ulceration from the disease may increase the risk and susceptibility for transmission of HIV.

Fig. 7.11 Chancroid. Multiple small, painful ulcers or chancres, with a purulent base are characteristic of chancroid.

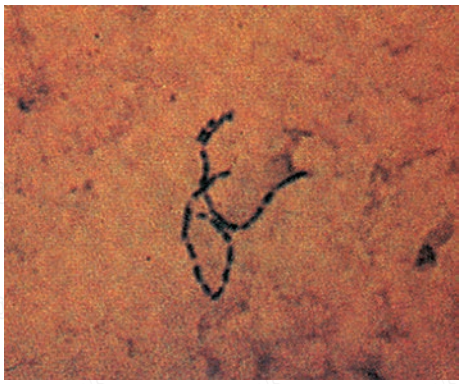

Fig. 7.13 Chancroid. The purulent exudates can be collected and stained with Wright's stain and show a chain of coccobacilli in a characteristic "school of fish" pattern.

Fig. 7.12 Chancroid. Multiple painful coalescing ulcerations on the penile shaft.

Fig. 7.14 Chancroid. The painful ulcers may elongate and coalesce, and bubo may form in the inguinal fold.

Genital Warts (Condyloma Acuminata)

Description

- Genital warts are due to infection of genital or perianal skin by the human papillomavirus (HPV).
- Warts in these locations can be difficult to evaluate clinically, are difficult to eradicate, frequently recur, and can lead to carcinoma.
- Genital warts are especially worrisome in immunocompromised patients.

History

- Warts may spread rapidly over moist areas and may therefore be symmetric on opposing surfaces of the labia or rectum.
- Common warts can be the source of genital warts, although they are usually caused by different types of virus (HPV).
- Genital warts can be difficult to treat and frequently recur after treatment.
- Latent virus exists beyond the treatment areas in clinically normal skin.
- Half of patients who have multiple and widespread infection with genital HPV and who practice orogenital sex have oral condylomata. The lesions are asymptomatic. Magnification may be necessary to detect oral lesions.
- The course is highly variable. Spontaneous resolution may occur but warts may persist for long periods.

Skin Findings

- Genital wart lesions may vary from person to person.
- Lesions tend to be pale pink to white or light brown and are rough, barely raised papules.
- Some lesions may have small finger-like projections on a broad base.
- The surface may be smooth, velvety, and moist, and it lacks the hyperkeratosis of warts found elsewhere.
- The lesions may coalesce in the rectal or perineal area to form a large, cauliflower-like mass.
- Warts may extend into the vaginal tract, urethra, and rectum, in which case a speculum or sigmoidoscope is required for visualization and treatment.

Fig. 7.15 Genital wart at the urethral meatus.

Fig. 7.16 Genital warts spread rapidly over moist areas, such as under the foreskin and on the vulva, and tend to be more numerous than on skin in other areas.

Differential Diagnosis

- Pearly penile papules are dome-shaped, frond-like or hair-like projections that appear on the corona of the penis and sometimes on the shaft, just proximal to the corona. They occur in up to 10% of male patients (these small angiofibromas are normal variants but are sometimes mistaken for warts)
- Molluscum contagiosum (a dome-shaped, firm, white papule that usually has a central depression)

Fig. 7.17 Genital warts. Grouped and clustered flesh-colored to light-brown plaques have a verrucous texture, characteristic of human papillomavirus infection.

Fig. 7.18 Genital warts. Pink papules with vascular changes are seen at the meatal opening of the penis.

Treatment

- Magnification may be required to make the diagnosis because some warts are flat, inconspicuous, and difficult to visualize.
- Treatment can be difficult, and multiple visits and procedures are often necessary for success.
- Liquid nitrogen cryotherapy can be performed. The wart is frozen until a rim of 1 mm appears around it. Repeat treatment is performed in 2 to 3 weeks. The treatment is painful, and blisters may form.
- Electrocautery and curettage involves a light touch with monopolar electrocautery; this is effective for treating a few isolated lesions, but scarring is possible.
- Podofilox (Condylox gel) is applied to the external genital warts twice a day for 3 days consecutively, followed by 4 days without treatment. This cycle is repeated at weekly intervals for a maximum of 4 weeks. Local adverse effects of the drug, such as pain, burning, inflammation, and erosion, have occurred in more than 50% of patients.
- Imiquimod cream 5% is an immune response modifier. It is applied every other night at bedtime, left on the wart for 8 to 12 hours, and removed by washing with mild soap and water. This regimen is repeated until the warts have resolved, which

Fig. 7.19 These genital warts are similar in appearance to common warts.

Fig. 7.20 Multiple discrete genital warts are seen on the shaft of the penis.

Fig. 7.21 Genital warts are pale pink with numerous, discrete, narrow to wide projections on a broad base.

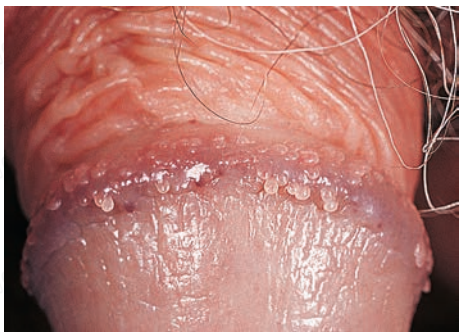

Fig. 7.22 Pearly penile papules are an anatomic variant of normal, most commonly found on the corona of the penis. They are sometimes mistaken for warts. No treatment is required.

usually takes 2 to 3 months. Treatment may have to be temporarily interrupted if irritation occurs. There are many treatment failures.

- Sinecatechins 15% ointment—apply 0.5 cm per wart three times a day for a maximum of 16 weeks.
- The use of condoms may reduce transmission to partners who are likely to be uninfected (e.g., new partners).

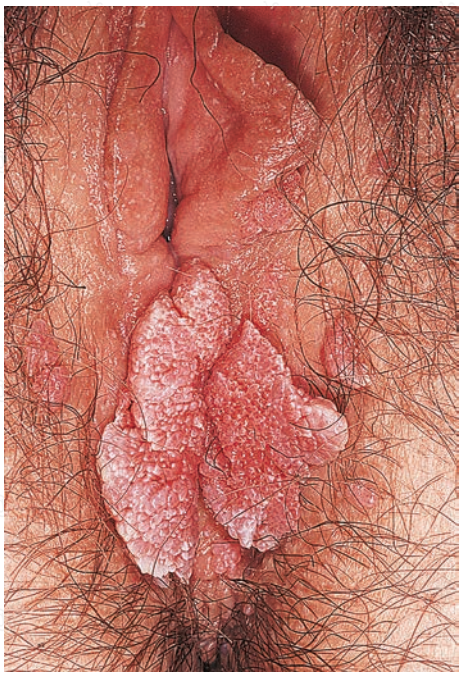

Fig. 7.23 Genital warts. A large cauliflower-like wart projects from the vagina. Warts in the anal area may be numerous and very large. Infection to this extent is painful.

Fig. 7.24 Genital warts. Podophyllin or imiquimod (Aldara) would be reasonable initial therapy. Consider excision if topical therapy fails.

- More than 95% of cervical carcinomas are related to HPV infection.
- For this reason women who have no visible external warts, but have a sexual partner with genital warts, should have a complete gynecologic examination and a Papanicolaou (Pap) smear.

Pearls

- Individual variations in cell-mediated immunity may explain differences in severity and duration.
- Warts occur more frequently, last longer, and appear in greater numbers in people with AIDS or cancer and in those who are taking immunosuppressive medications, such as transplant recipients.
- Genital warts can be prevented in males and females with vaccines, such as Gardasil and Cervarix. Gardasil protects against HPV types 6, 11 (90% of genital warts), and 16 and 18 (up to 70% of cervical cancer cases). Vaccination is indicated for young women and men aged 9 to 26 years, a three-shot series is given over 6 months.
- Ceravix is active against HPV types 16 and 18. Data from clinical trials suggest that the vaccine also offers protection against other virus types responsible for causing cervical cancer, including HPV types 31, 33, and 45, the next most common cancer-causing strains. Cervarix is approved for use in girls and women aged 10 through 25 years to prevent cervical cancer. It is a three-shot series given over 6 months.

Pediatric Considerations

- The rates of perinatal transmission from mother to child are not known and are likely to be lower than previously thought.
- Genital warts that are seen in children younger than 3 years can be perinatally acquired from the mother and do not necessarily indicate child abuse.
- If genital or anal warts are seen in older children if sexual abuse is suspected, the child should be referred to a sexual abuse team to investigate further sexually transmitted infections and the possibility of sexual abuse.
- The presence of genital warts does not "prove" sexual abuse, and HPV typing is generally not helpful.

Fig. 7.25 Anal warts are often numerous and very large. The patient responded to the application of 20% podophyllin in benzoin that was applied in the physician's office.

Fig. 7.26 Anal warts. Many small warts may be found in the anal area. Topical therapy or electrocautery should be effective.

Fig. 7.27 Anal warts. Cauliflower-like verrucae with linear fronds and folds are seen in the crural folds of the vulva.

Genital Herpes Simplex

Description

- Genital herpes simplex is a common sexually transmitted disease caused by the herpes simplex virus.
- The primary infection is followed by recurrent outbreaks of grouped vesicles on an inflamed red base.
- Many cases are transmitted by people who are unaware that they have the infection or are asymptomatic when transmission occurs.

History

Primary Infection

- After a total of 3 to 15 days after exposure, influenza-like systemic signs begin, such as fever, headache, and myalgias, and symptoms peak 3 to 4 days after the grouped vesicles develop.
- Tender lymphadenopathy occurs in the second and third weeks after initial infection.

Fig. 7.28 Primary herpes simplex. A combination of small intact pinpoint vesicles are seen on an inflamed base with a more advanced painful ulceration where vesicles and pustules have coalesced and have become necrotic.

Fig. 7.29 Primary herpes simplex. Small, painful 1- to 2-mm papules are seen on the penile shaft early in the course of a herpes simplex infection.

Fig. 7.30 Primary herpes simplex. Polymorphic shallow erosions have yellow exudate surrounding the perianal area.

Recurrent Infection

- Influenza-like symptoms are less intense or most often absent with recurrent infections.
- The prodrome is described as pain, burning, tingling, or itching in the infected area.
- A chronic relapsing course is common for most patients.

Skin Findings

- Symptoms of a primary infection are more severe (greater number of lesions) and more extensive than recurrent infection.

Fig. 7.31 Recurrent herpes simplex. Very small, 1-mm dry crusted grouped erosions, 3 to 5 days after the initial herpes infection.

Fig. 7.32 Primary herpes simplex. Herpetic erosions and crusted macules surround the vulva.

- The lesions in recurrent infection occur in the same region and sequence but on a diminished scale.
- The condition presents with a red swollen plaque followed by grouped vesicles that evolve into pustules.
- The pustules rupture or break, may crust, and then form shallow, painful erosions.
- Large confluent erosions and ulcers can occur.
- The lesions heal in 2 to 4 weeks; recurrent lesions heal in 1 to 2 weeks.
- Hypopigmentation, hyperpigmentation, and sometimes scars may be left behind.
- Primary infection is often the most extensive and severe in women; lesions are seen on the labia majora and minora, perineum, and inner thighs. Infections may also occur on the labia and buttocks.
- Regional lymphadenopathy (painful) occurs with primary infection.

Fig. 7.33 Recurrent herpes simplex. Multiple umbilicated vesicles are spread over a large surface area on the vulva and inguinal fold.

Fig. 7.34 Primary herpes simplex. Numerous lesions form on moist surfaces.

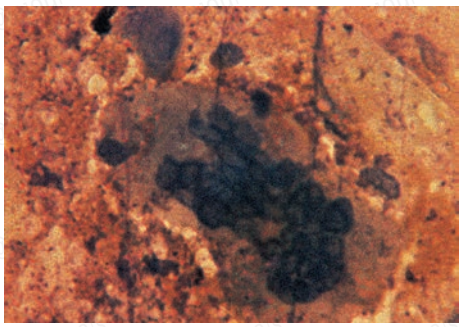

Fig. 7.35 Primary herpes simplex. Tzanck smear shows multinucleated giant cell.

Fig. 7.36 Primary herpes simplex. Lesions spread over a wide area.

Fig. 7.37 Primary herpes simplex. Vesicles became confluent and then eroded.

Laboratory and Testing

- The most definite method of diagnosis is a viral culture.
- Lesions must be sampled in the vesicular or early ulcerative stage.
- A rapid test is the Tzanck smear, which is best obtained from intact vesicles. Multinucleated giant cells are the characteristic finding.
- A rapid direct fluorescent antibody (DFA) examination is more readily available at most hospital laboratories.
- An intact vesicle can undergo biopsy for histologic confirmation, but this is not as accurate as culture or antibody testing.

Differential Diagnosis

- Syphilis
- Chancroid

Treatment

Counseling

- There is currently no permanent cure for herpes simplex.
- The natural history of the disease, the potential for recurrent episodes, asymptomatic viral shedding, and sexual transmission should be explained.
- The patient should be instructed to use condoms during all sexual exposures with new or unaffected sex partners.
- Condoms are not 100% effective in protecting males.
- Vaginal secretions may infect males on the thighs and pubic areas, especially the base of the penis.

Systemic Therapy

- Systemic antiviral drugs may partially control the symptoms and signs of herpes eruptions.
- These drugs neither eradicate latent virus nor affect the risk, frequency, or severity of recurrences after the drug is discontinued.

Primary Infection

- Treatment should be initiated within 72 hours of the onset of signs and symptoms. One of the following drugs can be used:
  - Valacyclovir (Valtrex) 1 g every 12 hours for 7 to 10 days.
  - Famciclovir (Famvir) 250 mg every 8 hours for 7 to 10 days.
  - Acyclovir (Zovirax) 200 mg every 4 hours five times a day, 400 mg every 8 hours, or 800 mg orally every 12 hours for 7 to 10 days.
- Cool, wet water dressings may suppress inflammation.
- Severe primary infections can be treated intravenously with acyclovir 5 mg/kg every 8 hours for 7 days. This regimen should be considered in immunocompromised patients.

Fig. 7.38 Recurrent herpes simplex. Vesicles are seen on a red base.

Recurrent Infection

- Treatment with one of the following regimens is initiated within 24 to 48 hours of the onset of signs and symptoms:
  - Valacyclovir (Valtrex) 500 mg every 12 hours for 3 days.
  - Valacyclovir (Valtrex) 1 g once a day for 5 days.
  - Famciclovir (Famvir) 125 mg every 12 hours for 5 days.
  - Acyclovir (Zovirax) 400 mg every 8 hours for 5 days.

- Patients should be provided with a prescription for the medication so that treatment can be started at the first sign of prodrome or genital lesion.

Long-Term Suppressive Therapy

- Valacyclovir (Valtrex) 1 g daily or 500 mg daily can be prescribed for fewer than nine recurrences a year.
- Famciclovir (Famvir) 250 mg twice daily.
- Acyclovir (Zovirax) 400 mg twice daily.
- Treatment is continued for at least 6 to 12 months.
- If treatment is successful, a trial without medication may be considered.
- Daily suppressive therapy reduces the frequency of genital herpes recurrences by at least 75% among patients who have frequent recurrences (six or more occurrences per year).
- Suppressive treatment reduces but does not eliminate asymptomatic viral shedding.

Reducing the Risk for Transmission

- Valacyclovir (Valtrex) 500 mg taken once daily by immunocompetent persons with recurrent genital herpes simplex virus type 2 infection significantly reduces the rates of viral transmission of genital herpes to a susceptible partner.

Fig. 7.39 Recurrent herpes simplex. A group of vesicles are seen on a red base.

Fig. 7.40 Recurrent herpes simplex under the foreskin. A group of discrete erosions is present. Crusts do not form on this moist surface.

Fig. 7.41 Primary herpes simplex. Multiple oral mucosal erosions are seen.

Table 7.1 Treatment of Genital Herpes (Oral)

Condition	Recommended Regimens
First Clinical Episode	• Acyclovir 400 mg orally three times a day for 7–10 days OR • Acyclovir 200 mg orally five times a day for 7–10 days OR • Valacyclovir 1 g orally twice a day for 7–10 days OR • Famciclovir 250 mg orally three times a day for 7–10 days *Treatment can be extended if healing is incomplete after 10 days for all of the above therapies.
Suppressive Therapy for Recurrent Genital Herpes	• Acyclovir 400 mg orally twice a day OR • Valacyclovir 500 mg orally once a day* OR • Valacyclovir 1 g orally once a day OR • Famciclovir 250 mg orally twice a day *Valacyclovir 500 mg once a day might be less effective than other valacyclovir or acyclovir dosing regimens in persons who have very frequent recurrences (i.e., ≥10 episodes per year).
Episodic Therapy for Recurrent Genital Herpes	• Acyclovir 400 mg orally three times a day for 5 days OR • Acyclovir 800 mg orally twice a day for 5 days OR • Acyclovir 800 mg orally three times a day for 2 days OR • Valacyclovir 500 mg orally twice a day for 3 days OR • Valacyclovir 1 g orally once a day for 5 days OR • Famciclovir 125 mg orally twice daily for 5 days OR • Famciclovir 1 g orally twice daily for 1 day OR • Famciclovir 500 mg once, followed by 250 mg twice daily for 2 days
HIV Infection **Daily Suppressive Therapy in Persons With HIV**	• Acyclovir 400–800 mg orally twice to three times a day OR • Valacyclovir 500 mg orally twice a day OR • Famciclovir 500 mg orally twice a day
HIV Infection **Episodic Infection in Persons With HIV**	• Acyclovir 400 mg orally three times a day for 5–10 days OR • Valacyclovir 1 g orally twice a day for 5–10 days OR • Famciclovir 500 mg orally twice a day for 5–10 days

Data from Centers for Disease Control and Prevention Guidelines, 2015; http://www.cdc.gov/std/tg2015/herpes.htm.

Pubic Lice (Pediculosis Pubis)

Description

- Pubic lice is the most contagious sexually transmitted disease in humans.
- Direct contact is the primary source of transmission.
- The chance of acquiring the pubic lice parasite from an infested partner is more than 90%.

History

- Fomite transmission occurs from sheets and clothing.
- Most patients complain of pruritus or a crawling sensation.
- Many patients are aware that something is crawling on the groin but are not familiar with the disease and have never seen lice.
- The individual louse parasites are quite small and difficult to see.
- Up to 30% of patients infested with pubic lice have at least one other sexually transmitted disease.

Skin Findings

- Lice may be difficult to see with close inspection or magnification.
- Eggs (nits) are firmly cemented to hair shafts 1 cm from the skin surface and usually hatch in 8 to 10 days.
- The pubic hair is the most common site of louse infestation, but lice frequently spread to the hair around the anus as well.
- On hairy individuals, lice may spread to the upper thighs, abdominal area, axillae, chest, and beard.
- Occasionally, gray to blue macules (maculae ceruleae) that vary in size from 1 cm to 2 cm are seen in the groin and at sites distant from the infestation.
- Most infected patients have very little if any inflammatory changes, but those who delay seeking help may develop widespread inflammation and infection of the groin with regional adenopathy.

Standard Treatments

- For most cases of pubic lice, topical medications, in the form of rinses, shampoos, and lotions, are effective standard treatments.
- Over-the-counter permethrin rinse 1% (Nix cream rinse) is often the drug of first choice for the treatment of lice. It is applied and washed off after 10 minutes.
- Pyrethrin shampoos (RID, A-200, R&C) are also used in a similar manner to rinses.
- Permethrin 5% cream (Elimite) is prescribed when over-the-counter treatment fails. It is left on the hair overnight.
- Lindane shampoo (Kwell) is left on for 5 minutes and then washed out; treatment is repeated in 1 week. It is a prescription medication, used if over-the-counter treatments fail. Lindane-resistant lice have emerged in recent years. Lindane is not recommended in pregnant women and children younger than 2 years.
- Malathion 0.5% lotion (Ovide) is highly effective prescription medication. It is applied to dry hair and shampooed out after 8 to 12 hours.
- For most of the previous topical treatments, one should wash the affected area, towel dry,

Pediatric Considerations

- Infested adults may spread pubic lice or crab lice to the eyelashes of prepubertal children.
- Sexual abuse is a possible cause of crab lice infestation in prepubertal children.

Fig. 7.42 *Phthirus pubis* (pubic louse, or crab louse). The crab louse is the smallest louse, with a short oval body and prominent claws resembling those of sea crabs.

then saturate hair with medication. Leave pyrethrin and permethrin on for 10 minutes, but leave Lindane on for 4 to 5 minutes. Thoroughly rinse away medication. Nits will not be removed with the previous topical applications. A nit comb is helpful for removing the nits. One should put on clean clothing and underwear and machine-wash all clothing, bedding, and towels. One should also inform sexual partners of the risk, and one should refrain from sexual contact until treatment is complete.

- All agents attack the louse nervous system, but nits are not affected.
- Treatment should be repeated in 1 week to kill nits that have not hatched.
- Oral medication with ivermectin 200 µg/kg/day is given in a single oral dose that is repeated in 1 to 2 weeks. The average adult dose is 12 mg. It attacks invertebrate nerve and muscle cells in the louse and causes paralysis and death. It has selective activity against parasites but no systemic effects on mammals.

Nit Removal

- It is important to remove all nits.
- One may remove them with fingernails, with nit comb, or by clipping or shaving hair completely.
- Shaving the pubic and abdominal hair may be helpful in severe or recalcitrant cases.
- Fomite control is essential.

Fig. 7.43 Almost translucent crab louse parasites can be seen attached to pubic hair shafts, feeding on the host, with numerous white to yellow nits tightly adhering to surrounding hair shafts.

Molluscum Contagiosum

Description

- Molluscum contagiosum is a poxvirus infection of the skin characterized by discrete umbilicated papules.
- It is considered a sexually transmitted disease when occurring in the genital area of adults.

History

- Molluscum contagiosum is very common in children.
- It is spread by direct contact or by autoinoculation.
- Lesions tend to be more numerous and spread rapidly in patients with atopic dermatitis or erythematous skin.
- Lesions may become large, numerous, and disfiguring in patients with HIV. It is often a marker of late-stage HIV disease.

Skin Findings

- Molluscum contagiosum lesions are 2- to 5-mm discrete, pink to flesh-colored, umbilicated dome-shaped papules.
- The pubic and genital areas are most commonly involved in adults.
- The lesions are frequently grouped and cover a wide area.
- Inflammation, erythema, and scaling at the periphery of a single or several lesions may occur. This may be the result of inflammation from scratching, or it may be a hypersensitivity reaction.
- Trauma may decrease the characteristic appearance of some lesions.
- Papules are often camouflaged by pubic hair. Most patients have just a few lesions that can be easily overlooked.
- The focus of examination is the pubic hair, genitals, anal area, thighs, and trunk. Lesions may appear anywhere except the palms and soles.

Differential Diagnosis

- Warts and flat warts
- Nevi
- Milia
- Sebaceous glands (hyperplasia)

Treatment

- Genital lesions should be treated to prevent spread through sexual contact.
- New lesions too small to be detected at the first examination may appear after initial treatment and require attention at a subsequent visit.
- Small papules can be quickly removed with a curette with or without local anesthesia. Bleeding is controlled with gauze pressure. Curettage is useful when there are a few lesions because it provides the quickest, most reliable treatment, but may be too painful for small children. A small scar may form; therefore this technique should be avoided in cosmetically important areas.
- Lidocaine–prilocaine (EMLA) cream applied 30 to 60 minutes before treatment helps prevent the pain of curettage for children.
- Cryosurgery with liquid nitrogen is effective for patients who do not object to the discomfort. The papule is sprayed or touched lightly with a nitrogen-bathed cotton swab until the advancing, white, frozen border has progressed down the side of the papule to form a 1-mm halo on the normal skin surrounding the lesion. This should take approximately 5 seconds. A conservative approach is necessary because excessive freezing produces hypopigmentation or hyperpigmentation.

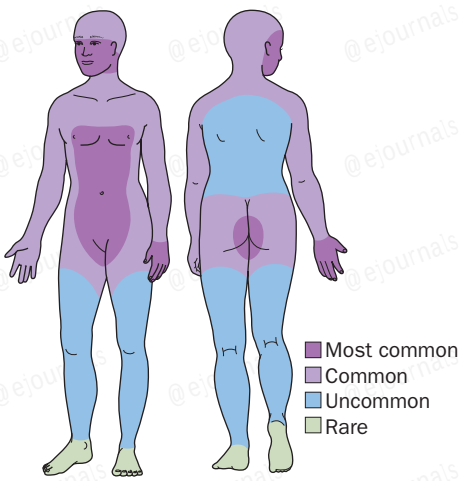

Fig. 7.44 Molluscum contagiosum distribution diagram.

Fig. 7.45 Molluscum contagiosum. Lesions are usually discrete, white, and dome-shaped. They lack the many small projections found on the surface of warts.

Fig. 7.46 Molluscum contagiosum. Close observation of individual lesions is necessary to confirm the diagnosis. Lesions are often misdiagnosed as warts.

Fig. 7.47 Molluscum contagiosum. Molluscum are difficult to see through pubic hair. These lesions were removed with a number one curette.

- A small drop of cantharidin 0.7% (Cantharone) is applied with the stick end of a cotton swab over the surface of the lesion, and contamination of normal skin is avoided. This should be washed off 4 to 6 hours later. Lesions blister and may resolve without scarring. New lesions occasionally appear at the site of the blister created by cantharidin. Hypopigmentation or hyperpigmentation may occur.
- Imiquimod 5% cream (Aldara) can be effective when applied three times weekly at night for 2 to 3 months. This is especially effective for treating facial molluscum in children when scarring procedures are contraindicated.
- In atopic dermatitis patients with molluscum, the dermatitis must also be treated at the same time because the altered skin barrier will promote autoinoculation.
- MolluscumRx is blend of plant extracts. It does not blister or burn the skin. The treatment is painless. It is applied twice a day. It is not reliably effective.

Pediatric Considerations

- Genital molluscum contagiosum is common in children and this finding alone does not warrant further evaluation for sexual abuse.
- One should look for other evidence of molluscum in other regions and in other siblings, especially if they bathe together.
- Children with molluscum contagiosum should not bathe with their siblings.
- Cantharone should not be used on the face.

Fig. 7.48 Molluscum contagiosum. Molluscum are commonly found in the genital area in young children. Individual lesions can become inflamed.

Fig. 7.49 Molluscum contagiosum. Molluscum are commonly found in the pubic area in adults. Examine this area with magnification. The hair obscures the view, and many lesions can be hidden.

Fig. 7.50 Molluscum contagiosum. A single lesion became inflamed and disappeared 10 days later.

Fig. 7.51 Molluscum contagiosum. Molluscum spread rapidly over warm, moist intertriginous areas on the upper thigh near the vulva.

Viral Infections 8

Kathryn A. Zug

Warts (Verruca Vulgaris)

Description

- Warts are benign epidermal proliferations caused by human papillomavirus (HPV) infection, a double-stranded DNA virus, which infects skin and mucous membranes.
- There are more than 150 different types of HPV. New subtypes are defined by DNA hybridization. Some subtypes are associated with a particular location and characteristic clinical and pathologic presentation.
- Transmission is by simple contact, often at sites with small skin breaks, abrasions, or other trauma. The virus must contact basal epithelial cells for infection to occur.
- Local spread is often by autoinoculation.

History

- The estimated incidence of infection is 10% in children and young adults.
- The peak incidence is age 12 to 16 years.
- The incubation period is variable: 1 to 6 months for common warts.

Skin Findings

- Flesh-colored papules evolve into dome-shaped, gray to brown, hyperkeratotic, discreet and rough papules, often with black dots on the surface.
- The black dots are thrombosed capillaries.
- Warts are usually few in number but may be numerous.
- Common sites are the hands, periungual skin, elbows, knees, and plantar surfaces.
- Filiform warts are growths with finger-like, flesh-colored projections on a narrow or broad base; they often occur on the face.

Laboratory

- HPV subtyping is not routine, readily available, or necessary for common warts. Subtype associations are:
  - Common warts with HPV 2, 4, 7.
  - Plantar warts with HPV 1, 4.
  - Genital warts with HPV 1, 2, 6, 10, 11, 16, 18, 31, 32, 33, 34.
  - Genital HPV subtypes 16, 18, and 31 are high-risk subtypes and account for approximately 75% of invasive genital cancers.
- A nonresolving wart on the hand, periungual unit, or the foot should be biopsied to rule out squamous cell carcinoma, which can mimic a wart, particularly in the region of the nail unit.

Course and Prognosis

- The course is highly variable; spontaneous resolution with time and the development of a cell-mediated immune response is the rule.
- In children approximately two thirds of all warts spontaneously regress within 2 years.
- Warts in the immunocompromised patient can be widespread, intractable, and chronic.

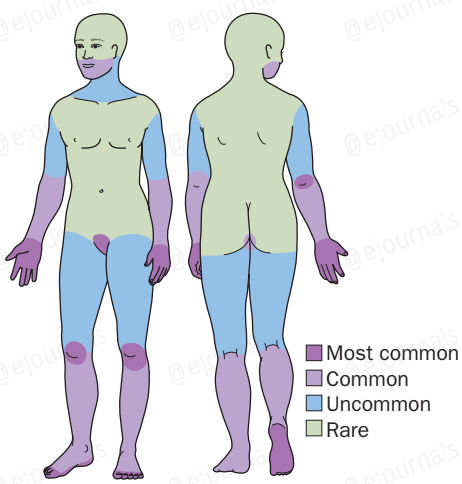

Fig. 8.1 Warts distribution diagram.

Fig. 8.2 Warts form cylindric projections. The projections become fused in common warts on thicker skin and form a highly organized mosaic pattern on the surface.

Fig. 8.4 Warts. Thrombosed black vessels become trapped in the projections and are seen as black dots on the surface. They bleed when pared with a blade.

Fig. 8.3 Warts remain confined to the epidermis and interrupt normal skin lines. The wart is gone when normal skin lines reappear.

Fig. 8.5 This digitate wart has a single projection that resembles a finger.

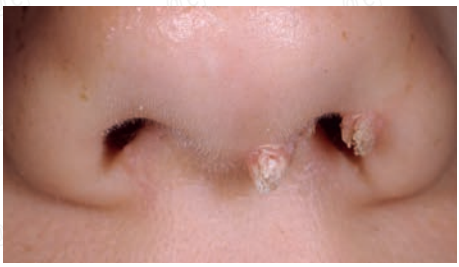

Fig. 8.6 Digitate warts in the nostril area of a young child. Nose picking and trauma should be avoided as spread by picking may occur.

Treatment

- Multiple treatments are available for warts. No single treatment is consistently highly effective. Painful treatment should be avoided, especially in children. Because warts will resolve spontaneously with no treatment, this may be comfortably recommended; however, many patients seek treatment because of the unsightly appearance, fear of spread or enlargement, or discomfort from pressure.
- Over-the-counter topical salicylic acid preparations (15%–40%) are applied once a day; they are safe and effective. The preparations may be occluded with tape to increase penetration. The duration of treatment is often lengthy (8–12 weeks). Soreness and irritation are minor side effects. Cure rate with salicylic acid preparations is 75%, compared with 48% with placebo. Some options are Mediplast (40% salicylic acid), DuoFilm solution (17% salicylic acid) or patch (40% salicylic acid), and Occlusal-HP solution (17% salicylic acid).

Fig. 8.7 Filiform wart with finger-like projections. These are most commonly observed on the face.

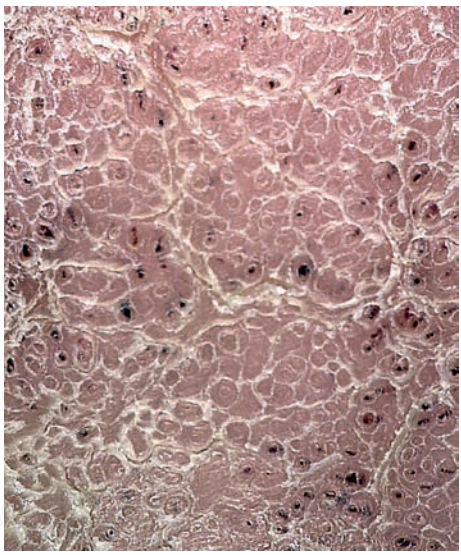

Fig. 8.8 Warts. Rough, frond-like surface is made up of cylindrical projections of epidermis.

Fig. 8.9 Multiple common warts between the fingers. Treating a few at a time, rather than all, will often allow immunity to develop, resulting in regression of all warts.

Fig. 8.10 Warts. The hands are the most commonly involved area. Warts become confluent and obscure large areas of normal skin. Biting or picking the skin around the nails can spread the warts.

- Soak a piece of cotton in vinegar (any color), apply to the surface of the wart, and cover with tape. Remove the tape in the morning. Repeat each night until the wart clears. Use less frequently if irritation occurs.
- Multiple visits and treatments are often necessary for success when treating with ablative therapy. With liquid nitrogen cryotherapy, the 15-second freeze time is repeated once. A follow-up visit for retreatment occurs in 2 to 3 weeks. Cure rate in the range of 52% is reported. Side effects are pain and a blister after treatment. Use caution when treating warts around the nail unit. Older children may tolerate gentle cryotherapy; consider this for long-standing warts or if other child-friendly treatments have failed.
- Imiquimod 5% cream (Aldara) is an immune response modifier with limited use in common warts; efficacy is limited by poor penetration in nonmucosal skin. Treat with liquid nitrogen, then apply a 17% salicylic acid preparation at night, and imiquimod in the morning with occlusion. Continue for

6 to 9 weeks. Efficacy is 50% to 100% anecdotally.
- The limitations of electrocautery and curettage are pain, secondary infection, and scarring.
- The limitations of laser surgery are pain and potential scarring. Pulsed dye laser has been used but shows no significant advantage over conventional treatment.
- Filiform warts are the easiest to treat. Local anesthesia can be used and the lesion removed with a snip or a curette. Light electrocautery and cryotherapy are other alternatives.

Pearls

- Individual variations in cell-mediated immunity may explain differences in wart severity and duration.
- Warts remain confined to the epidermis and interrupt normal skin lines. The wart is gone when normal skin lines reappear.

Pediatric Considerations

- Warts are common in children. Treatment—if offered—should be child-friendly; painful therapy should be avoided.
- Biting, shaving, or picking the wart-infected skin can spread warts. Inform your patients and discourage them from these habits.
- Warts occur more frequently, last longer, and appear in greater numbers in patients with AIDS or lymphoma and in patients on immunosuppressive medications.

Table 8.1 Different Types of Human Papillomaviruses and Their Clinical Manifestations

Clinical Manifestation	HPV Types
Plantar warts	1, 2, 3, 4, 27, 29, 57
Common warts	1, 2, 3, 4, 27, 57
Flat warts	3, 10, 28
Epidermodysplasia verruciformis	5, 8, 9, 12, 14, 15, 17, 19–25, 36, 47, 50
Genital warts, laryngeal papillomas	6, 11
Butcher's warts	7
Focal epithelial hyperplasia (Heck's disease)	13, 32
Anogenital dysplasias and neoplasms (rarely laryngeal carcinomas)	16, 18, 31, 33, 35, 42, 43, 44, 45, 51, 52, 56, 58, 59, 68
Keratoacanthoma	37
Cutaneous squamous cell carcinoma	38, 41, 48
Oral papillomas, inverted nasal papillomas	57
Buschke–Löwenstein tumors	6, 11
Bowenoid papulosis	16, 18, 33, 39
Cystic warts	60
Pigmented wart	65
Vulvar papilloma	70
Oral papillomas (in HIV-infected patients)	72, 73
Common wart in renal allograft recipient	75–77
Cutaneous wart	78

Fig. 8.11 Filiform and digitate warts consist of a few or several finger-like flesh-colored projections emanating from a narrow or broad base. They are most commonly observed about the mouth, the beard, eyes, and nose.

Fig. 8.12 Warts on the palms have a similar appearance to those on the soles. The skin is thick, and the warts are more difficult to treat with liquid nitrogen and salicylic acid.

Fig. 8.13 These warts have become confluent. Freezing a wide area of the fingertip is very painful. Localized areas should be treated in two or three treatment sessions.

Fig. 8.14 Warts are frozen until the "freeze front" extends for about 1 to 2 mm beyond the growth. Using two freeze–thaw cycles during one treatment session may increase the cure rate.

Fig. 8.15 Warts blister 1 or 2 days after freezing with liquid nitrogen. The size of the blister varies depending on the location and the individual. Blisters are often filled with blood and are painful. These may be punctured and drained with a #11 surgical blade.

Fig. 8.16 Warts. Oral papillomatous proliferation on the anterior hard palate in a patient with HIV infection and oral papillomavirus infection.

Fig. 8.17 Warts. Large hemorrhagic bullae can form on the backs of the hands after treatment with liquid nitrogen.

Fig. 8.18 The wart virus spread to the edge of the blister and formed a wart larger than the lesion that was originally treated. This is one possible side effect of cryosurgery.

Fig. 8.19 Warts are often grouped and are easily spread by scratching. The surface projections in these warts are very small and require magnification to be seen.

Fig. 8.20 Common warts around the periungual skin are unsightly and difficult to treat. Cuticle biting or emery board use may spread periungual warts.

Fig. 8.21 Periungual warts. The proximal nail folds are involved. Nail biting spreads warts about the fingernails.

Fig. 8.22 An undesirable result of liquid nitrogen freezing is recurrence of the warty growth at the periphery of the treated area.

Fig. 8.23 "Kissing lesions." Warts on one toe have spread to the adjacent toe. Apposition of the two surfaces would enhance the effect of salicylic acid liquid.

Flat Warts

Description

- Flat warts are benign cutaneous hyperproliferations due to infection with HPV. Common subtypes are types 3 and 10.

History

- Flat warts are common in children and young adults.
- Flat warts spread in a local region often through mildly traumatized skin, such as within an area of shaving.

Skin Findings

- These pink, light brown, or light yellow papules are slightly elevated and flat-topped. They vary in size from 0.1 to 0.3 cm. They may be few or numerous and often occur grouped or in a line as a result of spread from scratching.
- Typical sites are the forehead, back of the hands, chin, neck, and legs.
- Flat warts are typically asymptomatic.

Course and Prognosis

- The duration may be lengthy; flat warts may be very resistant to treatment. They are generally located in cosmetically important areas, where aggressive, scarring treatment procedures must be avoided.
- Immunocompromised patients often have a protracted course.

Treatment

- For sparse numbers of lesions, a salicylic acid preparation may be applied daily directly to each lesion. This treatment is limited by irritation.
- Imiquimod 5% cream (Aldara) is applied to affected skin at night. Decrease frequency of application if excessive irritation occurs. Treatment may be required for weeks.
- Tretinoin cream 0.025%, 0.05%, or 0.1% is applied at bedtime over the entire involved area. The frequency of application is adjusted to produce fine scaling and mild erythema. Treatment may be required for weeks or months.
- Liquid nitrogen or a very light touch with an electrocautery needle may be performed for quick results. Flat warts may not respond to cryotherapy, even after many treatment sessions.
- Applied once or twice a day for 3 to 5 weeks, 5-fluorouracil cream 5% (Efudex) may produce dramatic clearing of flat warts. Persistent hyperpigmentation may follow the use of 5-fluorouracil and is minimized by applying it to individual lesions with a cotton-tipped applicator.

Pearls

- Inform patients that flat warts are easily spread within areas of shaving. Shaving over affected skin should be discouraged.
- Unlike common warts, the face is a common location for flat warts.
- Imiquimod appears promising in the treatment of flat warts; its use may be limited by high cost and erythema and skin discomfort. Use is off-label.

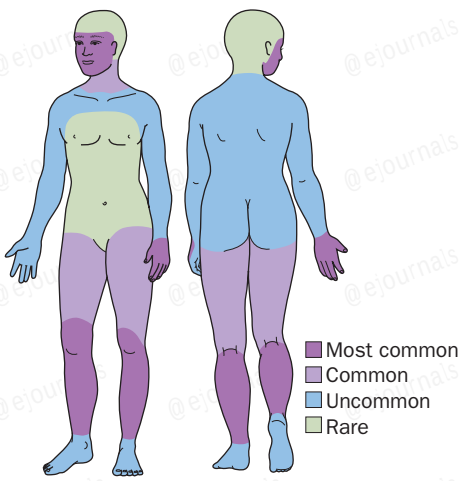

Fig. 8.24 Flat warts distribution diagram.

Fig. 8.25 Numerous flat warts occurring individually, grouped, and some demonstrating a linear spread, likely along an area of skin damage, such as a scratch.

Fig. 8.26 This degree of dissemination of flat warts is not usually seen in persons with normal cell mediated immunity; HIV infection should be considered.

Fig. 8.27 Scattered pink, smooth, flat-topped flat warts.

Fig. 8.28 The face is a commonly involved site. Flat warts are difficult to treat. Many different modalities may be tried, and the goal is resolution of the warts without scarring. Imiquimod is a helpful and useful new addition to treatment options; use is titrated to avoid severe inflammation but to achieve resolution of the warts. Use is off-label for flat warts.

Plantar Warts

Description

- Plantar warts are caused by HPV infection on the plantar foot.
- Warts frequently occur at points of maximal pressure, such as over the heads of the metatarsal bones, the heels, or the toes.
- A cluster of many warts is referred to as a "mosaic wart."

Skin Findings

- The round, single or multiple, coalescing, flesh-colored, rough keratotic papules often look depressed.
- Punctate black dots within the wart, often seen on paring, are capillary loops.
- The papules may be tender with pressure.
- Some plantar warts are depressed, resembling numerous small pits.

Laboratory

- Biopsy may be indicated in warts that are rapidly growing, ulcerated, atypical, or resistant to treatment; squamous cell carcinoma or melanoma may mimic a wart.
- HPV types 1, 2, and 4 are typically associated with plantar warts.

Course and Prognosis

- Treatment is often difficult; plantar warts can be very refractory and recurrent. Often, multiple treatment sessions are required.
- Hyperhidrosis is associated with a more widespread distribution of warts that are often refractory to treatment.

Treatment

- Plantar warts do not require therapy as long as they are painless. Spontaneous resolution with time is the rule.
- There are multiple treatment options, indicating no single best option.
- Keratolytic therapy with salicylic acid (DuoPlant, Occlusal) is a conservative initial treatment. There is no scarring. The wart is pared, the affected part is soaked in warm water, and the salicylic acid preparation is applied to the wart surface. Limitations include irritation and soreness. Treatment may require 6 to 8 weeks.
- Plasters with salicylic acid 40% (Mediplast) are useful in treating plantar warts. They are left on for 24 to 48 hours and replaced. Treatment may require 6 to 8 weeks.
- Imiquimod 5% cream (Aldara) may help hasten resolution; one method is to use cryotherapy first, then apply imiquimod every night under duct tape occlusion for 6 to 12 weeks.
- Blunt dissection is a fast, effective surgical treatment (90% cure rate) and usually produces no scarring. It is superior to both electrodesiccation/curettage and excision because normal tissue is not disturbed. Many podiatrists are experienced at this procedure.
- In cryosurgery with liquid nitrogen, the nitrogen is applied for 15 to 30 seconds, twice to a wart. The resultant painful blister can interfere with mobility. Repeated light applications of liquid nitrogen are optimal. Treatment is painful.
- Soak a piece of cotton in vinegar (any color), apply to the surface of the wart, and cover with tape. Remove the tape in the morning. Repeat each night until the wart clears. Use less frequently if irritation occurs.
- Carbon dioxide and pulsed dye laser treatment is also available but is expensive and probably no more effective than other treatments.
- Electrodesiccation/curettage is sometimes used; it is infrequently chosen because of pain from the anesthesia, postoperative pain, and a risk for scarring.
- Diluted intralesional cidofovir may play a treatment role for large, recalcitrant warts.

Pearls

- A clavus (corn) can be mistaken for warts.
- A wart lacks surface skin lines and has centrally located black dots that bleed with paring. Corns have a hard, painful, translucent central core.

- Gentle paring of a wart to remove debris or using a pumice stone to whittle away debris improves penetration of topical therapies.
- Caution your patient not to pick at the warty skin, and to clean any paring tool so not to spread wart virus from the débrided skin to other areas.
- Persistence in treating plantar warts can pay off; the slow process of salicylic acid débridement can take as long as 12 weeks to resolve a wart.

Pediatric Considerations

- Choose a painless treatment option (duct tape occlusion or salicylic acid) or no treatment for plantar warts in children; in time, the warts will resolve spontaneously.
- Aggressive treatment is not appropriate; it can result in marked pain, difficulty walking, scarring, and fear of future medical care providers.

Fig. 8.29 This plantar wart was shaved to reveal pinpoint black areas of hemorrhage.

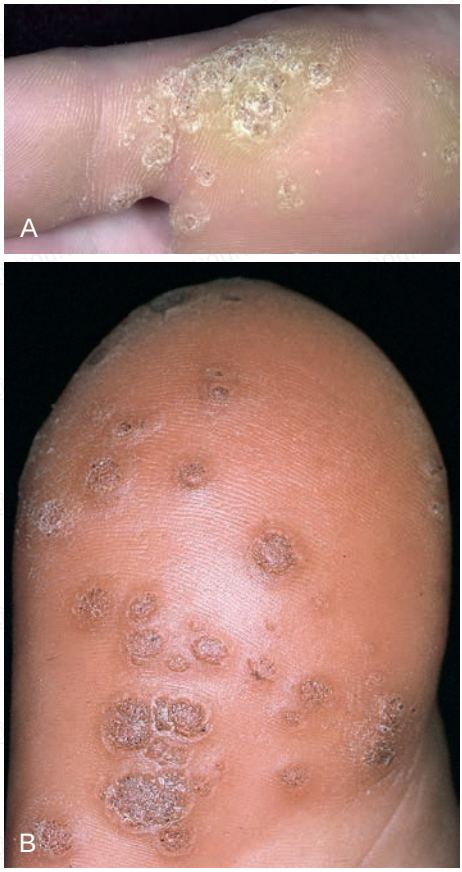

Fig. 8.30 Multiple plantar warts are a difficult management problem. It is best to treat a few at a time to try to stimulate an endogenous immune response.

Fig. 8.31 A shaved surface of a plantar wart reveals numerous pinpoint black areas, which are capillary loops.

Molluscum Contagiosum

Description

- Molluscum contagiosum is a localized, self-limited viral infection of the skin; it is spread on the skin by autoinoculation and is transmitted to others by skin-to-skin contact.
- The cause of infection is a DNA virus of the poxvirus family.

History

- Molluscum contagiosum may occur at any age.
- Numerous lesions and ease of spread are notable in atopic patients.
- It peaks in between 3 and 9 years of age and again between 16 and 24 years.
- Lesions tend to occur in different areas of the body within different age groups.
- Most lesions are asymptomatic, although tenderness and itching can occur and are usually associated with mild local inflammation.
- Lesions are transmitted by close contact.

Skin Findings

- Molluscum contagiosum begins as a 1- to 2-mm shiny, white to flesh-colored, dome-shaped firm papule.
- There is a small central whitish umbilication (depression) that is best seen with magnification or when the epidermis is lightly frozen with ethyl chloride or liquid nitrogen.
- Over some weeks, the lesion maintains its discrete dome shape with central punctum, attaining a maximum size of 2 to 5 mm.
- With time, the papule becomes softer and pinker, and the central umbilication becomes more obvious.
- Untreated lesions usually persist for 6 to 9 months before slowly involuting, not usually leaving any mark, but rarely a minute pitted scar remains.
- Inflammation surrounding a lesion of molluscum contagiosum implies a host immune response and predicts resolution. The inflammation can be robust and mimic abscess or infection.
- Excoriations, as well as crusting from secondary impetiginization, may be present.
- The body area involved varies with age.
- Children tend to have lesions on the upper trunk, extremities, and especially on the face.
- Larger lesions occur in immunocompromised hosts.
- Numerous lesions may be seen in atopic individuals with eczematous or xerotic skin.

Laboratory

- Skin biopsy is rarely needed to establish the diagnosis in an immunocompetent host. Clinical lesions are characteristic.
- Biopsy confirms the presence of large intracytoplasmic viral inclusions known as "molluscum bodies" within infected keratinocytes.
- Curettage of a lesion expresses a white, rubbery core of infected keratinocytes suitable for potassium hydroxide examination.
- Infected keratinocytes are strikingly round and separate easily from one another.
- Normal keratinocytes are flat and cohesive, forming a sheet of adherent cells.
- Lesions occurring in an immunocompromised host, such as those

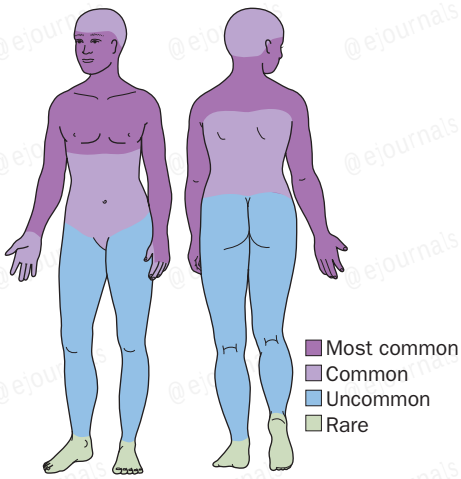

Fig. 8.32 Molluscum contagiosum distribution diagram.

infected with HIV, should be biopsied to confirm the diagnosis. Other infections that also occur in such patients may mimic molluscum contagiosum.

Course and Prognosis

- Individual lesions often resolve spontaneously within 6 to 9 months but may persist for years.
- Individuals with atopic dermatitis are prone to developing numerous lesions within eczematous areas through autoinoculation of inflamed skin. Such lesions are notoriously difficult to clear until the eczema is brought under control.
- Molluscum contagiosum is similarly difficult to treat in immunocompromised hosts, such as in the setting of HIV. Lesions are often more numerous and widespread, and individual lesions can become quite large and persistent.

Differential Diagnosis

- Differential diagnosis of molluscum lesions in immunocompetent hosts includes:
  - Flat warts
  - Genital warts
  - Herpes simplex virus (HSV) infection
- Warts lack the central umbilication and may occur on the palms and soles
- Herpes lesions are vesicles that are only transiently umbilicated; they are usually tender and have a more rapid onset and shorter clinical course
- In patients with HIV infection, other opportunistic fungal infections, including cryptococcosis and histoplasmosis, may produce lesions resembling those of molluscum contagiosum

Treatment

- Skin-to-skin contact should be avoided to minimize transmission of the virus.
- Because lesions resolve spontaneously in healthy individuals and because there is some risk for scarring with treatment, the decision to treat must be made on an individual basis.
- In children, lesions should be kept covered by clothing if possible. Picking is discouraged.
- Genital lesions in sexually active adults should be treated (see Chapter 7).
- Sexual partners of affected individuals should be checked for lesions.
- Depending on the location of lesions, the patient should be advised not to shave lesional areas because it can also lead to autoinoculation.
- Curettage to remove the infectious central core of the lesions is fairly painless and clears the lesions. For refractory or resistant spreading lesions, this may be considered in children in a "pain-free" outpatient surgical environment.
- Anesthesia may not be required but is recommended, especially in children.
- There is some risk for scarring, and caution should be used, especially on the face.
- Conservative cryosurgery with liquid nitrogen is effective and, in trained hands, rarely produces scarring. Treatment can be painful, especially for genital lesions.
- Cantharidin 0.7% solution is painless, effective, and usually well tolerated, especially by children. A wooden stick applicator is used to cautiously place a drop on each lesion, in order to avoid normal skin. The treated lesion develops a small blister within 24 hours, which then resolves along with the lesion; scarring rarely occurs. A mild temporary burning pain may occur.
- Imiquimod 5% cream (Aldara), a topical immune response modifier, can be applied to the lesions daily (or less frequently depending on degree of irritation). Duration of treatment is up to 12 weeks. Resolution is variable with imiquimod.
- Hypoallergenic surgical adhesive tape may be used. The tape is applied to each lesion. The tape is changed each day after showering. Treatment is continued until the lesion has ruptured, which may require several weeks.
- Cimetidine may enhance lymphocyte proliferation and immune response. A small study showed it was effective in children. A dose of 40 mg/kg/day for 2 months appears to be of variable efficacy.
- MolluscumRx is blend of plant extracts. It does not blister or burn the skin. The

treatment is painless. It is applied twice a day. It is not reliably effective.

Pearls

- A drop of mineral oil on lesions and use of a magnifier or dermatoscope will often allow confirmation of the diagnosis by accentuating the lesion's central core.
- Treatment should be individualized; lesions are self-limited.
- Significant scarring may result from overtreatment.
- It is common to see erythema and scaling at the periphery of a single or several lesions. This may be the result of inflammation from scratching or may be a hypersensitivity reaction. Inflamed molluscum lesions often spontaneously clear coincident to the inflammation.

Pediatric Considerations

- Autoinoculation around the eyes is particularly common, especially in children. These lesions are best left to resolve spontaneously.
- Lesions will resolve spontaneously as cell-mediated immunity develops, so treatment is not absolutely necessary.
- If treatment is desired, the best options for treating molluscum in children include cautiously applied cantharidin, imiquimod, or low-strength tretinoin.
- Eutectic mixture of prilocaine and lidocaine (EMLA) or 4% lidocaine (LMX) should be applied 60 to 90 minutes before ablative procedures, such as liquid nitrogen or curettage.
- The dose of EMLA cream should be limited (especially in neonates and infants) because of the small risk for methemoglobinemia.
- Molluscum contagiosum is primarily a sexually transmitted disease in young adults.
- Lesions tend to occur on the lower abdomen, pubic area (including the genitalia), and thighs.

Fig. 8.33 Molluscum contagiosum. Multiple dome-shaped papules are seen on the face. Note the central umbilication filled with the infectious molluscum bodies.

Fig. 8.34 Scattered umbilicated papules in the region of the popliteal fossa in an atopic patient. The papules spread more easily on this compromised, inflamed atopic skin barrier.

Fig. 8.35 Molluscum contagiosum. Inoculation around the eye is a typical presentation for children.

Fig. 8.36 Molluscum contagiosum is characterized by discrete 2- to 5-mm, slightly umbilicated, flesh-colored, dome-shaped papules. It spreads by autoinoculation, by scratching, or by touching a lesion.

Fig. 8.37 Erythema surrounding several molluscum, some which have become necrotic. This inflammation is a sign of resolution of the lesions.

Fig. 8.38 Molluscum contagiosum. It is common to see erythema and scaling at the periphery of a single lesion or several lesions. This may be the result of inflammation from scratching, or may be a hypersensitivity reaction. Inflamed molluscum may clear spontaneously. This inflammation is often misinterpreted as infection.

Herpes Simplex (Cold Sores, Fever Blisters)

Description

- HSV is a double-stranded DNA virus with two different virus types (types 1 and 2) that can be distinguished in the laboratory.
- Type 1 is generally associated with vesicular ulcerative oral infections and type 2 with genital infections.
- Type 1 genital infections and type 2 oral infections are becoming more common, possibly as a result of increased incidence of oral–genital sexual contact.
- HSV infections have two phases: the primary infection, after which the virus becomes established in a nerve ganglion; and the secondary phase, characterized by recurrent disease at the same site.

Primary Infection

- Most primary infections are asymptomatic.
- The virus may be spread by respiratory droplets, direct contact with an active lesion, or contact with virus-containing fluid, such as saliva or cervical secretions, in people with no evidence of active disease.
- Symptoms occur 3 to 7 or more days after contact.
- Tenderness, pain, mild paresthesias, or burning occurs before the onset of lesions at the site of inoculation.
- Gingivostomatitis and pharyngitis are the most frequent manifestations of the first episode of type 1 infection.
- Localized pain, tender lymphadenopathy, headache, generalized aching, and fever are characteristic prodromal symptoms.
- Women with symptomatic primary genital infection may experience vulvovaginitis and vaginal and cervical erosions with pain, edema, and dysuria.
- Men or women may also experience proctitis, anorectal pain, discharge, constipation, or tenesmus.
- Grouped vesicles on an erythematous base appear and subsequently erode.
- The vesicles in primary herpes simplex are more numerous and scattered than in the recurrent infection.
- Lesions on the mucous membrane accumulate exudate, whereas lesions on the skin form a crust.
- Lesions last 2 to 6 weeks and heal without scarring.
- During this primary infection, the virus enters the nerve endings in the skin directly below the lesions and ascends through peripheral nerves to the dorsal root ganglia, where it remains in a latent stage.

Recurrent Infection

- The recurrence rate is the same as for patients who had a symptomatic or asymptomatic primary infection.
- Local skin trauma (e.g., ultraviolet light exposure, chapping, abrasion) or systemic changes (e.g., menses, fatigue, fever) reactivate the virus, which then travels down the peripheral nerves to the site of initial infection and causes the characteristic focal, recurrent infection.
- Recurrent infection is not inevitable. In many individuals, there is a rise in the antibody titer, but no clinical evidence or recurrence.
- The prodromal symptoms, lasting 2 to 24 hours, can resemble those of the primary infection. Tenderness, pain, mild paresthesias, or burning occurs before the onset of lesions in the focal area of the primary infection.
- Within 12 hours, a group of lesions evolves rapidly from an erythematous base to form papules and then vesicles.
- The dome-shaped, tense vesicles rapidly umbilicate.
- In 2 to 4 days, the vesicles rupture, forming aphthae-like erosions in the mouth and vaginal area or erosions covered by crusts on the lips and skin.
- Crusts are shed in approximately 8 days to reveal a pink, re-epithelialized surface.
- In contrast to the primary infection, systemic symptoms and lymphadenopathy are rare unless there is secondary infection.
- Many people experience a decrease in the frequency of recurrences with time, though some experience an increase.

Laboratory

- The polymerase chain reaction (PCR) assay detects viral DNA in specimens and has significantly improved the ability to diagnose HSV.
- PCR assay is quick, specific, and sensitive.
- Many virology laboratories have discontinued using cell cultures for these specimen types, making rapid PCR the gold standard for detection of HSV in genital and dermal specimens.
- Serology can be performed on blood specimens for identification of HSV types 1 and 2.

Differential Diagnosis

- Hand-foot-and-mouth disease
- Aphthous stomatitis
- Erythema multiforme
- Impetigo
- Herpes zoster

Course and Prognosis

- About 80% to 90% of people with a symptomatic first episode of type 2 genital infection will experience a recurrent infection within the next year, compared with 50% to 60% of patients with type 1 infection.
- An average of four recurrences a year occur in patients with type 2 infection, compared with one per year in type 1 genital infection.
- Other complications of HSV infection include ocular keratitis, encephalitis, meningitis, hepatitis, and pneumonitis.

Discussion

- HSV is the most common cause of genital ulcerations in the industrialized world. About one in five Americans has HSV type 2 infection.
- Most transmission of the virus occurs during periods of unrecognized, asymptomatic shedding of the virus.
- Infections can occur anywhere on the skin. Infection in one area does not protect the patient from subsequent infection at a different site.
- Herpes labialis (infection of the lips) is the most common presentation.
- Herpetic whitlow (herpes simplex of the fingertips) can resemble a group of warts or a bacterial infection. It is most often reported in pediatric patients with gingivostomatitis and in women with genital herpes.
- Herpes gladiatorum (cutaneous herpes in athletes involved in contact sports) is transmitted by direct skin-to-skin contact. This is a recognized health risk for wrestlers.
- Herpes simplex of the buttock area is more common in women.
- Herpes simplex of the lumbosacral region or trunk may be very difficult to differentiate from herpes zoster; the diagnosis becomes apparent only at the time of recurrence.
- Eczema herpeticum (Kaposi's varicelliform eruption) is the association of two common conditions: atopic dermatitis and HSV infection. The disease is most common in areas of active or recently healed atopic dermatitis, particularly the face, but normal skin can be involved. In most cases, the disease is a primary HSV infection. Herpes infections may spread within areas of other widespread dermatoses (Darier's disease); such spread may be camouflaged, heralded by an increase in lesional pain and worsening of disease with new erosions or crusted areas. The spread is more common on corticosteroid-treated skin and in the setting of immunocompromise.
- Herpes simplex genital lesions are a risk factor for transmission of HIV.
- Attempts to develop a preventive vaccine are ongoing; thus far, primary vaccination has been unsuccessful.
- HSV encephalitis may present as fever, headache, and confusion. It is the most common cause of sporadic encephalitis.

Treatment

- The patient should be advised of measures to prevent spread of the virus to others: contact with open lesions should be avoided; drinking vessels and razors should not be shared; condoms should be used; kissing while a lesion is open or has a moist crust may spread the disease.

- Infections resolve without treatment. The need for treatment of first-episode infections, recurrent infections, and suppressive therapy is based on each patient's needs.
- Long-term suppressive therapy can greatly improve the quality of life for people with frequent and painful recurrences.
- Subsequent recurrence rate off medication is not influenced by any topical or oral medication.
- See the following tables for CDC treatment recommendations: Table 8.2 for herpes simplex first episode, Table 8.3 for suppressive therapy, and Table 8.4 for treatment of recurrent genital infections, and Table 8.5 for recommended suppressive therapy in pregnant women.

Topical Agents

- These can be used for relief of pain. When applied frequently, tetracaine cream 1.8% (Cepacol Viractin Cream, which can be obtained over the counter) reduces the healing time of recurrent herpes labialis lesions by about 2 days.
- Abreva (docosanol) is a nonprescription topical cold-sore medication approved by the U.S. Food and Drug Administration (FDA). It shortens healing time to about the same extent as penciclovir cream.
- When applied several times each day, penciclovir cream (Denavir) reduces the duration of herpes labialis by about half a day. It is very expensive.

Table 8.2 CDC 2015 Recommended Regimens for First Clinical Episode Genital Herpes Simplex

Acyclovir 400 mg orally three times daily for 7–10 days, *or*
Acyclovir 200 mg orally five times daily for 7–10 days, *or*
Valacyclovir 1 g orally twice a day for 7–10 days, *or*
Famciclovir 250 mg orally three times a day for 7–10 days
Courtesy CDC.

Table 8.3 CDC 2015 Recommended Regimens for Suppressive Therapy for Recurrent Genital Herpes Simplex

Acyclovir 400 mg orally twice a day, *or*
Valacyclovir 500 mg orally once a day,* *or*
Valacyclovir 1 g orally once a day, *or*
Famciclovir 250 mg orally twice a day
*Valacyclovir 500 mg once a day might be less effective than other valacyclovir dosing regimens in persons with very frequent recurrences (>10 per year). Courtesy CDC.

Table 8.4 CDC 2015 Recommended Regimens for Recurrent Genital Herpes Simplex Infections

Acyclovir 400 mg orally three times a day for 5 days, *or*
Acyclovir 800 mg orally twice a day for 5 days, *or*
Acyclovir 800 mg orally three times a day for 2 days, *or*
Valacyclovir 500 mg orally twice a day for 3 days, *or*
Valacyclovir 1 g orally once a day for 5 days, *or*
Famciclovir 125 mg orally twice a day for 5 days, *or*
Famciclovir 1 g orally twice daily for 1 day, *or*
Famciclovir 500 mg once, followed by 250 mg twice daily for 2 days
Courtesy CDC.

Table 8.5 CDC 2015 Recommended Regimen for Suppressive Therapy of Pregnant Women With Recurrent Genital Herpes Infection*

Acyclovir 400 mg orally three times a day, *or*
Valacyclovir 500 mg orally twice a day
*Treatment recommended starting at 36 weeks' gestation, per American College of Obstetricians and Gynecologists. Courtesy CDC.

- Topical acyclovir is not approved for use on cold sores in the immunocompetent host because of its lack of efficacy. Use of topical antivirals may potentiate resistance to antiviral therapy, and because efficacy is lacking, such use should be discouraged.
- The lips should be protected from sun exposure with opaque creams, such as zinc oxide, or with sun-blocking agents incorporated into a lip balm.
- A wet dressing with cool water decreases erythema and débrides crusts to promote healing.

Oral Antiviral Agents

- Therapy is initiated at the first sign or symptom.
- Therapy is most effective when administered within 48 hours of the onset of signs and symptoms.
- The frequency and severity of episodes of untreated herpes may change over time. After 1 year of suppressive therapy, the frequency and severity of the infection should be re-evaluated to assess the need for continued therapy.
- Valacyclovir (Valtrex):
  - For initial episodes, 1 g is given twice a day for 7 to 10 days.
  - For recurrent episodes, 500 mg is administered twice a day for 3 days or 2 g two times in 1 day.
  - Suppressive therapy requires the administration of 1 g per day. In patients with a history of no more than nine recurrences a year, an alternative dose is 500 mg per day.
- Famciclovir (Famvir):
  - For initial episode: 250 mg is administered three times a day for 7 to 10 days.
  - For recurrent episodes, 125 mg is administered twice a day is given for 5 days.
  - For suppressive therapy, 250 mg is administered twice a day for up to 1 year.
- Acyclovir (Zovirax):
  - For initial episodes, 200 mg is given every 4 hours five times a day or 400 mg three times a day for 7 to 10 days.

Fig. 8.39 Herpes simplex. Recurrent infection results in tense, dome-shaped vesicles.

Fig. 8.40 Herpes simplex. The evolution of a group of herpetic vesicles is shown; the center appears depressed and sunken, "punched out."

  - For recurrent episodes, 400 mg is administered every 8 hours three times a day for 5 days.
  - For suppressive therapy, 400 mg is administered twice a day for up to 12 months. Then the case is re-evaluated.
  - Alternative regimens have included doses ranging from 200 mg three times a day to 200 mg five times a day.
- L-Lysine is ineffective.
- Long-term use of acyclovir topically or orally in people infected with HIV is a risk factor for the development of acyclovir resistance. Diagnosis of acyclovir-resistant viral lesions should be considered when lesions are longer in duration of healing.

Pearls

- Viral shedding occurs intermittently and in most cases without symptoms. It is the major cause of the ongoing epidemic.
- Umbilicated vesicles (dome-shaped with a slight central depression) are the hallmark of herpesvirus infections.
- Most infections are acquired from people who shed the virus but have no symptoms.

Fig. 8.41 Herpes simplex labialis. Coalescing grouped vesicles that have become purulent and are about to crust.

Fig. 8.42 Numerous erosions on the bottom lip during a primary herpes simplex infection.

Fig. 8.43 Recurrent herpes. A large group of vesicles appeared after sun exposure.

Pediatric Considerations

- Infants with suspected HSV infection should be treated with antiviral therapy and treated early to prevent disseminated infection.
- Infants who acquire the virus in utero have a poor prognosis with high morbidity (mental retardation, seizures, deafness) and high mortality rates.
- Infants who acquire the virus perinatally have a much better prognosis with more than 90% developing normally.
- The part of the infant's body that presents in delivery is most likely to come into contact with maternal virus-containing secretions and is more apt to show the first signs of infection.
- Cutaneous signs often lag behind other signs, such as poor feeding and irritability.
- Vesicles become umbilicated and cloudy and break in 8 to 12 hours to form a crust as the red base disappears.

Fig. 8.44 Eczema herpeticum is the association of two common conditions, atopic dermatitis and herpes simplex. The virus infects areas where atopic dermatitis is commonly found. The infection can spread rapidly over wide areas.

Fig. 8.45 Grouped vesicles on edematous, erythematous skin. This is an early outbreak of herpes simplex.

Fig. 8.46 Recurrent herpes with confluent vesicles starting to crust. Note the umbilication and central depression.

Fig. 8.47 Recurrent herpes on the finger. Herpes can infect any skin surface. A diagnosis of poison ivy was made, but the patient reported that this eruption had occurred several times in the past.

Fig. 8.48 Cutaneous herpes simplex on the buttocks occurs almost exclusively in women. The vesicles are grouped, on an erythematous base, and have become purulent.

Fig. 8.49 Eczema herpeticum. Umbilicated vesicles have spread widely over the face of a patient with active atopic dermatitis.

Fig. 8.50 Recurrent herpes. The diagnosis of herpes can be made at any stage in the evolution of lesions.

Varicella (Chicken Pox)

Description

- Varicella, a highly contagious infection, is caused by the varicella zoster virus (VZV) and most commonly results in lifetime immunity.
- It is caused by human herpesvirus type 3.
- See Table 8.6 for varicella vaccine recommendations.

History

- Transmission is via airborne droplets or rarely vesicular fluid.
- Patients are contagious from 2 days before the onset of the rash until all lesions have crusted.
- The incubation period is approximately 14 to 16 days.
- In children, prodromal symptoms are absent or consist of low-grade fever, headache, and malaise; fever, malaise, and a generalized vesicular rash develop and last 4 to 7 days. Photophobia may be present.
- Adolescents, adults, and immunocompromised persons have more severe disease and are at risk for complications.
- Moderate to intense pruritus is present during the vesicular stage.
- Temperature varies from 38° to 40° C but returns to normal when the vesicles disappear.

Skin Findings

- There is a simultaneous presence of lesions (vesicles, pustules, and crusts) in all stages.
- The rash begins on the trunk and spreads to the face and extremities. The extent of involvement variesconsiderably.
- A lesion starts as a 2- to 4-mm red papule, and then a thin-walled, clear vesicle appears on the surface. The vesicle becomes umbilicated (a central dell occurs) and cloudy, breaking after 8 to 12 hours to form a crust as the red base disappears. The formation of new lesions ceases by the fourth day.
- Crusts fall off in about 7 days and usually heal without scarring.
- Secondary infection or excoriation extends the process into the dermis.
- Vesicles often form in the oral cavity and vagina and rupture quickly to form multiple, aphthae-like ulcers.

Nonskin Findings

- Pneumonia is the most common serious complication in normal adults.
- Hepatitis is the most common complication in immunosuppressed patients.

Laboratory

- Culture or Tzanck's smear is performed for questionable cases.

Table 8.6 Immunization: Varicella Vaccine Recommendations (Varivax)

Persons <13 Years of Age	Persons >13 Years of Age
CDC recommends two doses of the chickenpox vaccine, first dose at 12–15 months of age and second dose at 4 through 6 years old	Two doses of varicella vaccine given 4–8 weeks apart are recommended for healthy adolescents and adults with no history of the disease
Children with a reliable history are considered immune	Those with a reliable history of previous infection are considered immune
Those with an uncertain history are immunized	Those who do not have such histories are considered susceptible and can be tested to determine immune status or can be vaccinated without testing
Serologic testing is not warranted because the vaccine is well tolerated in seropositive persons	

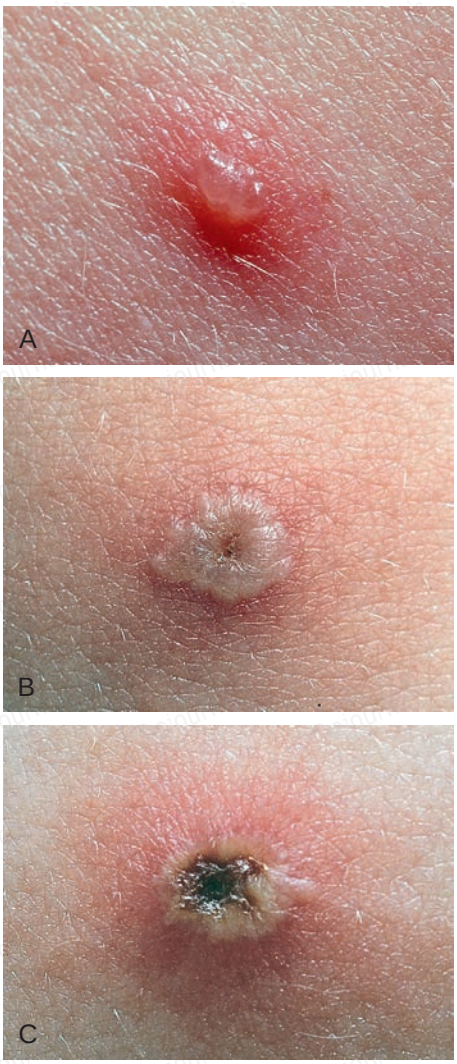

Fig. 8.51 A, Chicken pox—evolution of lesions. "Dewdrop on a rose petal." A solitary varicella vesicle. **B,** The vesicle becomes cloudy and umbilicated (depressed in the center). **C,** The vesicle forms a central crust.

- A direct immunofluorescence test of scrapings obtained from the vesicle base is a rapid and sensitive test, but not widely available.

Complications

- Bacterial superinfection with *Streptococcus pyogenes* or *Staphylococcus aureus,* pneumonia, dehydration, encephalitis, and hepatitis are possible complications. The most common neurologic complication is ataxia secondary to cerebellar inflammation. Roughly 15% of healthy adults develop pulmonary involvement.
- Because the association between Reye syndrome and aspirin use was identified, the occurrence of Reye syndrome has become more rare.
- Suspected ocular involvement should be evaluated by an ophthalmologist.
- Thrombocytopenia, transient thrombocytopenic purpura, and Henoch–Schönlein purpura are rare complications.
- Maternal infection with VZV during the first 20 weeks of gestation poses a risk for fetal congenital varicella syndrome (~2% risk). Perinatal infection can occur within 10 days of delivery. When infection of the mother occurs 5 days before or 2 days after delivery, infant mortality is 30%.

Fig. 8.52 Chicken pox. It is typical to have lesions all in one stage of development, as seen here. Fresh new crops of vesicles erupt over several days. The eruptive phase lasts about 4 days, and lesions crust by day 6.

Differential Diagnosis

- Disseminated varicella zoster
- Disseminated herpes simplex
- Eczema herpeticum
- Henoch–Schönlein purpura
- Smallpox
- Folliculitis
- Impetigo

Treatment

- Symptomatic treatment consists of bland antipruritic lotions (e.g., Sarna). Antihistamines (hydroxyzine) may help control excoriation.

Table 8.7 American Academy of Pediatrics Recommendations for Acyclovir Therapy of Varicella Zoster Virus Infections

Indications	Recommended Therapy
Nonpregnant, healthy adolescents ≥13 years of age who have varicella	Consider acyclovir: should be initiated within 24 hours of onset of rash
Children >12 months of age who have chronic cutaneous or pulmonary disorder or are on long-term salicylate therapy	Dosage: 20 mg/kg (800 mg maximum) orally four times a day for 5 days
Children receiving short, intermittent, or aerosolized courses of corticosteroids	Dosage: 20 mg/kg (800 mg maximum) orally four times a day for 5 days
Children infected from household contact	Dosage: 20 mg/kg (800 mg maximum) orally four times a day for 5 days
Healthy children and adults with complications of varicella	Intravenous acyclovir
Immunocompromised children (including secondary to high-dose corticosteroids) with primary varicella	Dosage: 10 mg/kg intravenously every 8 hours for 7 days
Immunocompromised children with recurrent zoster	IV acyclovir 10 mg/kg intravenously every eight hours for 7 days
Pregnant patients with complications of varicella	IV acyclovir 10 mg/kg intravenously every eight hours for 7 days
Healthy children with varicella	Routinely, no therapy
Pregnant patients with uncomplicated varicella	Routinely, no therapy
Healthy children exposed to varicella	Routinely, no therapy

Immunocompetent Patients

- Oral dosage:
  - Adults, adolescents, and children >40 kg: 800 mg 4 times per day for 5 days. Initiate therapy at the first signs of symptoms (i.e., within 24 hours). Treatment with acyclovir has been shown to shorten the time to healing, reduce the number of lesions, reduce the number of vesicles, and reduce other symptoms, such as fever, anorexia, and lethargy.
  - Children ≥2 years and ≤40 kg: 20 mg/kg/dose (not to exceed 800 mg) four times per day for 5 days. In general, acyclovir is not recommended for routine use for the treatment of varicella infections in otherwise healthy children at low risk for complications.
- Intravenous dosage:
  - Adults: In a case report, 20 mg/kg/day in three divided doses for 5 days was used successfully. Use ideal body weight when dosing obese patients.
  - Children ≥2 years and adolescents: 10 mg/kg/dose every 8 hours for 7 to 10 days or 1500 mg/m^2/day in three divided doses for 7 to 10 days.

Immunocompromised Patients

- Immunosuppressed patients (HIV patients) treated with acyclovir have decreased morbidity from visceral dissemination; there is a modest effect on cutaneous disease. The recommended schedule is acyclovir 10 mg/kg given intravenously (IV) every 8 hours for 7 to 10 days. The Centers for Disease Control and Prevention (CDC) recommend 10 to 15 mg/kg IV every 8 hours for 7 to 10 days in HIV-infected patients with severe or complicated disease. These patients can then switch to oral therapy (including acyclovir, famciclovir, or valacyclovir) after

Fig. 8.53 Numerous intensely pruritic crusted vesicles on the face. The lesions of varicella typically begin on the face, then spread to the trunk and extremities.

defervescence if there is no evidence of visceral involvement.

Pearls

- In varicella (chicken pox), lesions of different stages (vesicles, crusts, and pustules) are present at the same time in any given body area. This is in contrast to the rash of variola (smallpox), in which lesions are all in the same stage during the eruption course. Smallpox lesions are the same size and extend into deep dermis.
- In chicken pox, lesions are centripetal (more heavily distributed on the trunk); however, in smallpox, lesions are centrifugal (more lesions on the face and extremities than the trunk).
- Varicella is highly contagious; patients hospitalized for complications or therapy require strict isolation procedures. Preventing transmission of varicella in health care settings is critical to protect those most at risk for complications (immunosuppressed patients, premature infants, pregnant women. See http://www.cdc.gov/chickenpox/hcp/healthcare-setting.html.
- Acyclovir-resistant varicella may occur in people infected with HIV on chronic topical or oral therapy and should be considered in cases of severe atypical or disseminated disease.

Pediatric Considerations

- The varicella vaccine is highly efficacious, with a 96% seroconversion rate in healthy children; the efficacy is 71% to 91%.
- Children who have been immunized with the live attenuated vaccine may develop a mild afebrile illness—varicella-like syndrome—consisting of erythematous macules and papules, and few vesicles, roughly 15 days after exposure. The lesions are much less numerous.

Table 8.8 Recommendations for the Use of Varicella Zoster Immunoglobulin for Postexposure Prophylaxis

Persons <13 Years of Age	Persons >13 Years of Age
Used for passive immunization of susceptible, immunocompromised children after substantial exposure to varicella or herpes zoster, including:	A healthy, unvaccinated adolescent or adult who has had substantial exposure and is determined to be susceptible
1. Children with primary and acquired immunodeficiency disorders	Varicella zoster immunoglobulin should be considered for susceptible pregnant women who have been exposed, in order to prevent complications of varicella in the mother, rather than to protect the fetus
2. Children with neoplastic diseases who are receiving immunosuppressive treatment	Note: If varicella is prevented through the use of varicella zoster immunoglobulin, vaccination should be offered later
3. Neonates whose mothers have signs and symptoms of varicella within 5 days before and 2 days after delivery	
4. Premature infants who have substantial postnatal exposure and who should be evaluated on an individual basis	

Varicella Zoster

Description

- Varicella Zoster, otherwise known as herpes zoster, is a cutaneous viral infection generally involving the skin of single or adjacent dermatomes.
- Herpes zoster results from the reactivation of VZV that entered the cutaneous nerves during an earlier episode of chicken pox.
- Shingles is another name for herpes zoster.

History

- This condition occurs during the lifetime of 10% to 20% of all people.
- People of all ages may be afflicted; the incidence increases with age.
- Patients with zoster are not more likely to have an unknown underlying malignancy.
- Zoster may be the earliest clinical sign of the development of AIDS in high-risk individuals.
- Age, immunosuppressive drugs, lymphoma, fatigue, emotional upsets, and radiation therapy have been implicated in reactivating the virus.
- Elderly people are at greater risk for developing segmental pain, which can continue for months after the skin lesions have healed.
- Patients with Hodgkin's lymphoma are uniquely susceptible to herpes zoster.
- The pain may simulate pleurisy, myocardial infarction, abdominal disease, or migraine headache and may present a difficult diagnostic problem until the characteristic eruption provides the answer.
- The constitutional symptoms of headache, photophobia, and malaise may precede the eruption by several days. Fever is uncommon. Regional lymphadenopathy may be present.
- An attack of herpes zoster does not confer lasting immunity, and it is not abnormal to have two or three episodes in a lifetime.

Skin Findings

- Pre-eruptive tenderness or hyperesthesia throughout the dermatome is a useful predictive sign.
- Pain, itching, or burning, generally localized to the dermatome, may precede the eruption by 4 or 5 days.

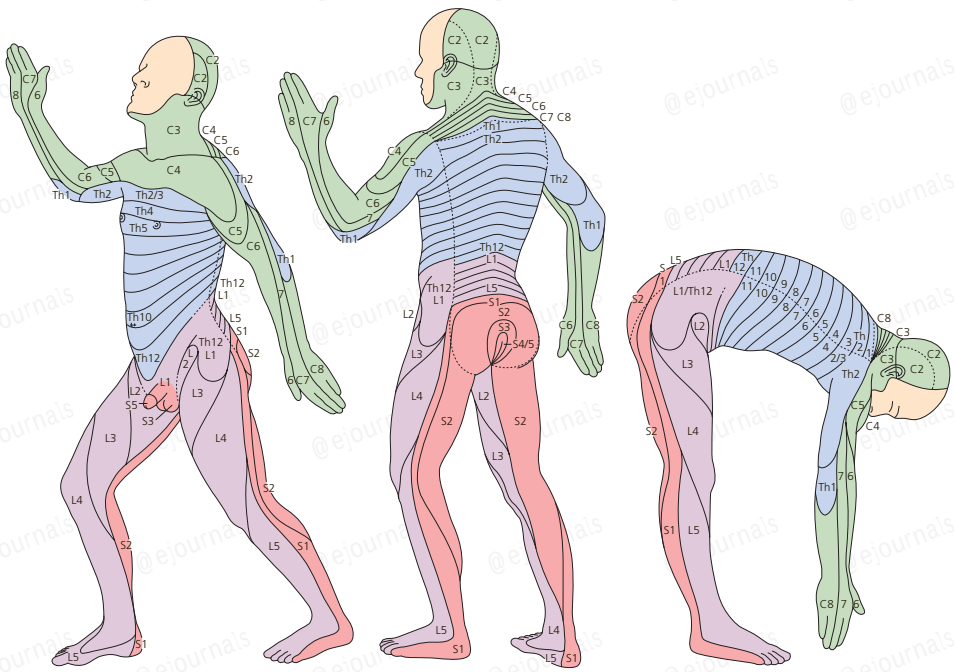

Fig. 8.54 Dermatomes.

- Although generally limited to the skin of a single dermatome, the eruption may involve one or two adjacent dermatomes. Noncontiguous multidermatomal lesions are most often associated with immunosuppressed individuals.
- Occasionally, a few vesicles appear across the midline.
- Approximately 50% of patients with uncomplicated zoster have a viremia, with the appearance of 20 or 30 vesicles scattered over the skin surface outside the affected dermatome.
- The thoracic region is affected in two thirds of cases.
- The eruption begins with red swollen plaques of various sizes and spreads to involve part or all of a dermatome.
- The vesicles arise in clusters from the erythematous base and become cloudy with purulent fluid by the third or fourth day.
- The vesicles vary in size, in contrast to the cluster of uniformly sized vesicles noted in herpes simplex.
- Vesicles either umbilicate or rupture before forming crusts, which fall off in 2 or 3 weeks.
- Elderly or debilitated patients may have a prolonged and difficult course. For them, the eruption is typically more extensive and inflammatory, occasionally resulting in hemorrhagic blisters, skin necrosis, secondary bacterial infection, or extensive scarring.
- Complications of herpes zoster in immune-competent individuals can include peripheral nerve palsies, encephalitis, myelitis, and a contralateral hemiparesis syndrome. Disseminated disease may result in death.
- Acute retinal necrosis, heralded by visual changes within weeks or months of an episode of zoster, is a complication more often associated with patients seropositive for HIV.

Ophthalmic Zoster

- Involvement of any branch of the ophthalmic nerve is called herpes zoster ophthalmicus.
- With ophthalmic zoster, the rash extends from eye level to the vertex of the skull but does not cross the midline.
- Vesicles on the side or tip of the nose (Hutchinson's sign) are associated with the most serious ocular complications.
- Of patients who are not treated with antiviral therapy, 50% will develop ocular

Fig. 8.55 Herpes zoster in an older woman in the thoracic dermatome. The pain before the eruption can be so intense that it is mistaken for a heart attack.

Fig. 8.56 Herpes zoster. Numerous grouped vesicles line the C3 to C4 dermatome on the right neck and postauricular skin. Herpes zoster typically affects only one or two dermatomes.

Fig. 8.57 An extensive eruption of zoster lines the chest and upper inner arm of a child (T2 dermatome). Note the grouped vesicles on patches of erythematous skin. Crops of vesicles erupt over 7 days, and crusts take 2 to 3 weeks to fall off.

complications (keratopathy, episcleritis, iritis). Oral antiviral therapy results in decreased frequency of late ocular complications.
- Patients with ophthalmic zoster should be referred to an ophthalmologist.

Postherpetic Neuralgia
- Pain is the major cause of morbidity in zoster; postherpetic neuralgia is pain that persists more than 30 days after the rash.
- The incidence and duration of pain increase with age.
- Pain can persist in a dermatome for months or years after lesions have disappeared.
- The pain is often severe, intractable, and exhausting. The patient protects areas of hyperesthesia to avoid the slightest pressure, which activates another wave of pain.
- Most patients younger than 30 years experience no pain. By age 40 years, the risk for prolonged pain lasting longer than 1 month increases to 33%. By age 70 years, the risk increases to 74%.
- The degree of pain is related neither to the extent of involvement nor to the number of vesicles or degree of inflammation or fibrosis in peripheral nerves.

Laboratory
- Culture is specific, but the virus is labile and not easily isolated.
- VZV serologic testing with PCR and genotyping is available through the CDC.
- Direct immunofluorescence of cellular material from skin lesions can be performed.
- For Tzanck's smear, the base of a vesicle is scraped with a cotton swab, and the material is smeared onto a glass slide. It is submitted to the laboratory or stained directly to see multinucleated giant cells.

Treatment
Suppression of Inflammation, Pain, and Infection
- Topical therapy is tried. Cool tap water can be used in a wet dressing. The wet dressings are applied for 20 minutes several times a day; they macerate the vesicles, remove serum and crust, and discourage bacterial growth.
- With oral steroids, there is a decrease of acute pain and a quicker rash resolution but no effect on postherpetic neuralgia. There is no difference in pain at 6 months when acyclovir and prednisone are used together, compared with acyclovir alone or prednisone alone. There are no significant differences between steroid-treated and non–steroid-treated patients in the time to a first or a complete cessation of pain. The incidence of adverse effects is higher in patients treated with corticosteroids.
- Sympathetic blocks (stellate ganglion or epidural) with bupivacaine 0.25% may terminate the pain of acute herpes zoster and prevent or relieve postherpetic neuralgia.

Attenuation of the Acute Phase
- Oral antiviral drugs decrease acute pain, inflammation, vesicle formation, and viral shedding.
- The duration and severity of postherpetic neuralgia may be reduced by treating acute herpes zoster with valacyclovir or famciclovir.
- Treatment is most effective when started within the first 48 hours of infection.
- It is reasonable to use antiviral therapy in the patient seeking medical treatment more than 48 hours after the vesicles appear if the lesions are not completely crusted.

- The recommended oral dosage for adults is a 7- to 10-day course of acyclovir (Zovirax) 800 mg five times a day; valacyclovir (Valtrex) 1000 mg three times a day; or famciclovir (Famvir) 500 mg three times a day. Valacyclovir and famciclovir are equal in their ability to increase healing and pain resolution; their simpler dosing regimen and pharmacokinetic profile make them preferable to acyclovir. All three drugs are safe and well tolerated. Dosage adjustments are necessary for patients with renal insufficiency.
- The drugs are given empirically to patients who are older than 50 years, are immunocompromised, or have trigeminal zoster.
- Topical antivirals play no role in the management of herpes zoster.

Postherpetic Neuralgia

Prevention

- Famciclovir and valacyclovir may decrease the duration of postherpetic neuralgia.
- Oral steroids used to prevent postherpetic neuralgia have not been proved effective.
- Some authors recommend starting amitriptyline at low doses (10–25 mg) and gradually increasing this to doses of 50 to 75 mg over 2 to 3 weeks in all patients older than 60 years as soon as shingles is diagnosed. A 50% decrease in the incidence of postherpetic neuralgia has been reported.

Treatment

- There is no reliable treatment for postherpetic neuralgia, which occurs in 10% to 15% of individuals, but in more than 60% of individuals 60 years and older. Consultation with a pain management specialist can be helpful.
- Oral analgesics (e.g., acetaminophen, oxycodone), the topical lidocaine patch, pregabalin (300 or 600 mg/day), or gabapentin (increase dose to tolerance; maximum, 3600 mg/day) are first-line treatments.
- Tricyclic antidepressants, such as amitriptyline 75 mg/day, nortriptyline (10–150 mg/day orally; start at low doses and gradually increase as needed), and desipramine (use doses of 10–25 mg orally at bedtime, and titrate to pain relief; in one study, the mean dose of desipramine after 6 weeks of treatment was 167 mg/day) are second-line drugs.
- Some clinicians advocate a short course of steroids (e.g., prednisone, 40–60 mg/day for 3–5 days or longer).
- Narcotics and analgesics are effective in many patients.
- Topical capsaicin cream (Zostrix, Zostrix HP) acts by enhancing the release or inhibiting the reaccumulation of substance P from cell bodies and nerve terminals. Patients experience some pain relief but may not be able to tolerate the burning. Applying EMLA or topical lignocaine (lidocaine) before capsaicin use may make the treatment more tolerable. Capsaicin should not be applied to unhealed skin lesions.

Varicella Vaccine

- Indicated for nonimmune compromised adults older than 60 years. Live attenuated virus vaccine reduces risk for shingles by 51% and reduces risk for postherpetic neuralgia by 67%. Single-dose treatment is recommended by the CDC, and is most effective in people aged 60 to 69 years (http://www.cdc.gov/vaccines).

Pediatric Considerations

- More than 20,000 healthy children in the United States will develop herpes zoster each year.
- Children with a history of chicken pox developing before age 1 year are at an increased risk for herpes zoster.
- Children with zoster do not have a higher incidence of underlying immune compromise; laboratory studies in healthy children with zoster are not routinely necessary.
- Otherwise healthy children with zoster do not require a serologic test for HIV.

Pearls

- Sacral zoster can occur. A neurogenic bladder with urinary hesitancy or urinary retention can be associated with zoster of the sacral dermatome S2, S3, or S4. Migration of virus to the adjacent autonomic nerves is responsible for these symptoms. Catheterization may be necessary.
- Varicella zoster of the geniculate ganglion is called Ramsay-Hunt syndrome. There is involvement of the sensory and motor portions of the seventh and eighth cranial nerves. There may be unilateral loss of taste on the anterior two thirds of the tongue and vesicles on the tympanic membrane, external auditory meatus, concha, and pinna. Other symptoms include tinnitus, vertigo, deafness, and ear pain.
- Herpes zoster in people infected with HIV is associated with frequent recurrences and atypical lesions. Treatment should be continued until all lesions have completely resolved.

Fig. 8.58 Herpes zoster. Coalescing, necrotic vesicles forming a cribriform necrotic ulcer on the scalp. Necrosis, a hallmark of infection severity, is more often seen in immunocompromised patients with herpes zoster.

Fig. 8.59 Sacral zoster. A neurogenic bladder with urinary hesitancy or urinary retention can be associated with zoster of the sacral dermatome S2, S3, or S4. Migration of virus to the adjacent autonomic nerves is responsible for these symptoms.

Hand-Foot-and-Mouth Disease

Description

- Hand-foot-and-mouth disease is a highly contagious viral infection that causes aphthae-like oral erosions and a vesicular eruption on the hands and feet. Children younger than 5 years are most commonly affected.
- The classical benign, self-limited form of this disease is associated with coxsackievirus A16.
- Enterovirus 71 is a picornavirus genetically related to coxsackievirus A16. It can cause a similar hand-foot-and-mouth disease, but epidemic outbreaks have associated potentially serious neurologic and cardiopulmonary complications, particularly in children younger than 4 years.
- Atypical coxsackievirus infections caused by coxsackievirus A6 have been reported in recent years with severe and extensive cases of hand-foot-and-mouth disease. Two thirds of cases occur in children younger than 2 years, and 24% occur in adults older than 18 years. Widespread vesicles involving the face and extremities, and bullae on the palms and soles, have been described. Systemic complications are rare.

History

- The incubation period is 1 to 7 days. Spread is by nose and throat discharge, saliva, and blister fluid.
- Coxsackievirus A16–related hand-foot-and-mouth disease usually presents with acute stomatitis and a mild fever. There may be a prodrome of mild symptoms, including sore throat and malaise or abdominal pain, for 1 or 2 days.
- About 20% of patients develop submandibular lymphadenopathy, cervical lymphadenopathy, or both.
- Epidemics usually occur in the summer and autumn but can appear at any time.
- Children younger than 5 years are most commonly affected, but the rate of infection among close household contacts is high. Good hand washing and surface disinfection may help reduce spread.
- Atypical coxsackievirus infection caused by coxsackievirus A6 is responsible for a growing number of severe, extensive cases.

Fig. 8.60 Hand-foot-and-mouth disease. Cloudy vesicles with a red halo are highly characteristic of this disease.

- Epidemics of disease associated with enterovirus 71–related disease have occurred in Bulgaria, Hungary, Malaysia, Taiwan, and Australia. Genotypes responsible for this disease in the Far East have arisen since 1997.
- Enterovirus 71 outbreaks commonly include fever, oral ulcers, extremity rash, vomiting, and cough.

Skin Findings

- The number of oral aphthae-like erosions (3–6 mm) varies from a few to 10 or more. They are irregularly distributed anywhere in the oral cavity. They are more painful in younger children. Each erosion lasts 3 to 5 days.
- Cutaneous lesions in coxsackievirus-induced hand-foot-and-mouth disease occur in two thirds of patients and appear less than 24 hours after the oral lesions. They begin as 3- to 7-mm red macules that rapidly become pale, white oval vesicles with red areolae. The vesicles have a unique rhomboidal shape

of "square blisters." There may be a few inconspicuous lesions, or there may be dozens.
- The vesicles occur on the palms, soles, dorsal aspects of the fingers and toes, and occasionally the face, buttocks, and legs.
- They heal in approximately 7 days, usually without crusting or scarring.
- Coxsackievirus A6 infection (atypical coxsackievirus infection) is most common before age 2 years and has perioral accentuation but is less likely to have intraoral involvement. Coxsackievirus A6 infection manifests with lesions beyond the palms and the soles, including the extremities and face. A Gianottii–Crosti syndrome–like eruption on the cheeks, extensor extremities, and buttocks, with truncal sparing, can be seen in more than one third of cases. Postdisease manifestations include desquamation of the palms and soles 1 to 3 weeks after infection and nail changes 4 to 6 weeks after infection.
- "Eczema coxsackium" (described with atypical coxsackievirus A6) is characterized by vesicles and erosions in previously affected areas of atopic dermatitis and can be mistaken for eczema herpeticum.
- Infants with coxsackievirus A6 (atypical coxsackievirus infection) may have large acral bullous involvement. Teens may have acral petechial or purpuric lesions.

Course

- Hand-foot-and-mouth disease caused by coxsackievirus A16 is usually mild and self-limited. It resolves without treatment and without scarring in about 10 days. Patients are most contagious during first 7 to 10 days of illness. Multiple routes of contagion include saliva, nasal secretions, respiratory droplets, fecal–oral route, and blister fluid. Oral ulcerations are painful in infants and interfere with feeding.
- Recent emergence of epidemics of hand-foot-and-mouth disease caused by enterovirus 71 are associated with varied neurologic syndromes, including aseptic meningitis, Guillain–Barré syndrome, polio-like paralysis, acute transverse myelitis, acute cerebellar ataxia, intracranial hypertension, and febrile convulsions. The prodrome is 1 to 7 days before the neurologic disease and has associated fever, coryza, malaise, headache, and diarrhea. Two thirds of those affected may have a rash; often truncal, herpangina-type lesions may occur in the mouth.

Pediatric Considerations

- Herpetic gingivostomatitis is the most common cause of stomatitis in children younger than 5 years. Gingival involvement is severe and associated with lymphadenopathy and a high fever. The oral erosions of hand-foot-and-mouth disease are usually small and uniform.
- Enterovirus 71 infection should be considered in the young child with neurologic manifestations (as described previously) and diffuse rash, sometimes petechial, or manifestations of herpangina.
- Outbreaks of hand-foot-and-mouth disease in day care centers are common. Viral shedding is prolonged (30 days in saliva, 60 days in feces) and requires cautious contact to prevent transmission.
- Supportive care measures include petroleum jelly (Vaseline) for skin lesions, zinc oxide barrier paste in the diaper area, hydration, and pain control with acetaminophen.

Laboratory

- The diagnosis is usually made clinically.
- Laboratory studies are usually unnecessary for the benign presentation of the disease.
- Virus can be cultured from the vesicles, throat, and stool. Viral isolates can be detected by neutralization assay.
- Convalescent sera show elevated titers of specific complement-fixing viral antibodies. Serum for serology can be examined for enterovirus 71–specific antibody by means of a serum neutralization assay, and may be detected in the sera of as many as 50% of acute and 70% of convalescent patients.
- Both varicella and herpes simplex have multinucleated, giant cells in smears taken from the moist skin exposed when a vesicle

is removed and the base scraped (Tzanck's smear). Giant cells are not present in the lesions of hand-foot-and-mouth disease.

Differential Diagnosis

- Herpangina (coxsackieviruses A1–10, 12, and 22l enterovirus 71; coxsackie B virus; adenovirus; echovirus) lesions are limited to the posterior oral cavity, tonsils, uvula, and soft palate; disease is associated with a higher temperature (101° to 104° F). It is most commonly spread by the fecal–oral route. Infants are most often affected. The incubation period is 2 to 5 days, and symptoms last 3 to 4 days. There is an increased risk for complications in pregnant women; these include preterm delivery, fetuses with low birth weight, and infants who are small for gestational age.
- Aphthous stomatitis (patients are afebrile and tend to have recurrences).

Treatment

- Children may be isolated during the most contagious period, usually for 3 to 7 days. Some may be carriers up to 3 months after the infection. Symptomatic relief is important in infants to prevent dehydration. Fever and pain are controlled with acetaminophen. Cool fluids are best tolerated; acidic foods are avoided.
- Acyclovir suspension 200 to 300 mg five times a day for 5 days is anecdotally reported to provide rapid relief of signs and symptoms in children aged 9 months to 5 years.
- Effective antiviral therapy for enterovirus 71–induced diseased is not presently available. Intravenous immunoglobulin has been of little benefit. Vaccine development is needed.

Pearls

- Cloudy gray-white vesicles with red halos on the palms and soles are highly characteristic.
- Increasing epidemics of enterovirus 71 disease in the Asia–Pacific Island region have been associated with severe neurologic and cardiopulmonary disease.
- Enterovirus 71 infection should be considered in the young child with fever, neurologic sequelae, and oral ulcers or extremity rash.
- Atypical coxsackievirus infection caused by coxsackievirus A6 is increasingly being reported.

Fig. 8.61 Hand-foot-and-mouth disease. Apthae-like erosions may appear anywhere in the oral cavity and are painful in infants and young children and may impede feeding.

Fig. 8.62 Hand-foot-and-mouth disease. Cloudy vesicles with red halos are highly characteristic of this disease.

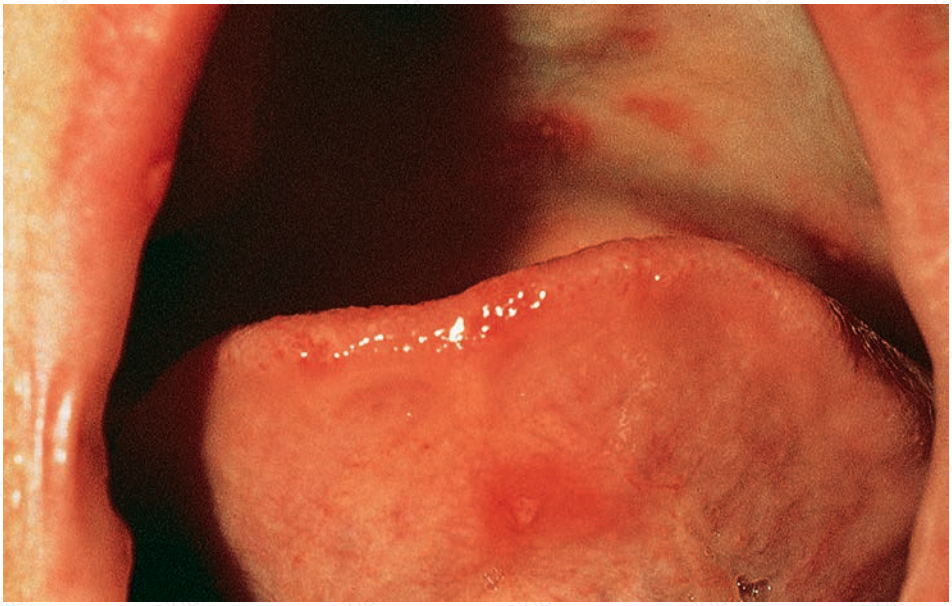

Fig. 8.63 Pale-white, oval vesicles with red areolae in hand-foot-and-mouth disease.

Zika Virus

Description

- Zika virus is caused by a single-stranded RNA flavivirus.
- The bite of an infected *Aedes* species mosquito is the primary source of infection.
- Zika virus was first discovered in Uganda, then spread to tropical Africa, Southeast Asia, and the Pacific Islands.
- It has caused outbreaks in South America and is deemed likely to continue to spread to new areas.
- Adverse outcomes in infants whose mothers have been infected during pregnancy are the reason prevention of infection is critical.
- Some cases of postinfection Guillain–Barré syndrome have been reported.

History

- Mild illness is characterized by acute onset of fever, itchy rash, joint pain, and conjunctivitis. Fever is mild and lasts only a day. Myalgia and headache occur in some patients, but many have minimal or no symptoms.
- Incubation period several days to a week. The symptoms are mild and last several days to a week.
- Infection during pregnancy can result in microcephaly and other fetal brain defects.

Skin Findings

- Conjunctivitis (red eyes) is most common.
- Maculopapular rash generally starts on the face on the first day of symptoms and spreads diffusely, peaking at day 2 or 3, then resolving. About 90% have a rash, and it is usually itchy.
- Rash can be morbilliform or scarlatiniform.

Laboratory

- Serum or urine testing is done by real-time reverse transcriptase PCR during the first week after onset of symptoms.
- Zika MAC-ELISA is another test authorized by the FDA for emergency use.
- State and local health departments can facilitate testing.

Treatment

- Treatment is supportive and includes rest, fluids, and acetaminophen as needed for fever and pain.
- Spread of disease may be prevented by avoiding more mosquito bites during the first week of infection.
- Fetuses and infants of women infected with Zika during pregnancy should be evaluated for congenital infection and neurologic abnormalities.

Pearls

- Zika symptoms are similar to the rash of dengue and chikungunya, which are also spread by *Aedes* species mosquitos. Patients suspected to have Zika should also be evaluated for those diseases because they have similar geographic distribution and symptoms.
- Mosquitoes that transmit Zika bite primarily during the daytime.
- Because there is no vaccine yet available, prevention of infection is through prevention of mosquito bites and prevention of sexual transmission by using condoms or not having sex.
- Long-sleeved shirts and long pants, window screens, and mosquito netting can help prevent bites.
- EPA-registered insect repellents containing DEET, picaridin, IR3535, oil of lemon, eucalyptus oil, or paramethane-3,8-diol are recommended by the CDC.
- After traveling to an affected region, even if symptom free, mosquito bites should be avoided to prevent possible spread of the virus.
- Zika virus stays in semen longer than blood; duration in semen not yet clear.

Pediatric Considerations

- Do not apply insect repellent to infants younger than 2 months.
- Proper clothing coverage for children helps prevent infection.
- Avoid the child's hands, mouth, and eyes, as well as any cuts, when applying repellant.

Fungal Infections 9

James G. H. Dinulos

Candidiasis (Moniliasis)

Description

- *Candida albicans* and a few other *Candida* species are capable of producing skin and mucous membrane infections.
- The organism lives among the normal flora of the mouth, vaginal tract, and lower gastrointestinal tract.
- *Candida* species reproduce through the budding of oval yeast forms, forming elongated pseudohyphae.
- Decreased cell-mediated immunity, compromised skin barrier, and changes in normal skin flora predispose to infection.
- Infancy, pregnancy, oral contraceptive use, systemic antibiotic therapy, diabetes, skin maceration, topical and systemic steroid therapy, and decreased cell-mediated immunity predispose to candidiasis.
- Patients develop satellite pustules at the edge of the rash, which is the hallmark of cutaneous candida.
- There are different clinical patterns, depending on the location of the infection.

Candida Balanitis

Description

- A localized, acute infection of the foreskin and glans penis caused by *Candida* species.

History

- Candida balanitis occurs more frequently in uncircumcised men.
- Diabetes increases the risk for candida balanitis.
- Sexual partners should be checked for candida infection.

Skin Findings

- Pinpoint red papules evolve into umbilicated pustules on the glans and coronal sulcus with pasty macerated debris under the foreskin.
- Pustules rupture under the foreskin and leave 1- to 2-mm, white doughnut-shaped superficial erosions. Erosions may progress to fissure or ulcerate.
- Edema and pain can be intense enough to limit retraction of the foreskin.

Laboratory

- Potassium hydroxide examination reveals numerous yeast forms.
- Bacterial culture should be performed when antifungal agents do not clear the rash.
- Consider a swab for herpes simplex polymerase chain reaction (PCR) testing.
- A skin biopsy should be done for severe or resistant cases.

Differential Diagnosis

- Herpes simplex
- Psoriasis
- Irritant contact dermatitis
- Plasma cell balanitis (Zoon's balanitis)
- Squamous cell carcinoma

Fig. 9.1 Candidiasis. The uncircumcised penis provides the warm moist environment ideally suited for yeast infection. Here, the inflammation is intense, causing fissuring. The white pasty exudate is highly characteristic.

Fig. 9.2 Candidal balanitis. Tender pinpoint red papules and pustules appear on the glans and are macerated by the overlying foreskin to form erosion.

Course and Prognosis

- Candida balanitis may be persistent and recurrent, especially in immunosuppressed patients (e.g., those with diabetes).

Treatment

- Topical therapies (miconazole, clotrimazole, ketoconazole, sertaconazole, oxiconazole, or econazole) should be applied twice daily for at least 10 days.
- Combination antifungal-steroid preparations (clotrimazole–betamethasone and nystatin–triamcinolone) should be avoided because of rebound redness and soreness.
- Severe candida balanitis should be treated with systemic antiyeast therapy (itraconazole 200 mg daily for 3–7 days or fluconazole 150 mg daily for 1–3 days).

Pearls

- Umbilicated pustules occur with herpes simplex and acute candida infection. They may be clinically indistinguishable.
- Satellite pustules and bright-pink papules are highly suggestive of candidiasis.
- Skin biopsies should be performed in persistent cases because squamous cell carcinoma in situ may mimic candida balanitis.

Fig. 9.4 Zoon's balanitis, or plasma cell balanitis, is a chronic inflammation of the penis in uncircumcised men and must be differentiated from candidal balanitis. Sometimes a skin biopsy is necessary.

Fig. 9.3 Candidiasis. Infection and inflammation are more intense on this warm and moist intertriginous surface.

Candida Diaper Dermatitis

Description

- *Candida* species can be a primary cause of diaper dermatitis, occurring as bright-red (beefy-red) plaques in the inguinal and gluteal folds.

History

- Diapers occlude the skin, leading to skin maceration and predisposing to skin infection and inflammation.
- Frequent diaper changes decrease the incidence of candida diaper dermatitis.
- Highly absorbent disposable diapers effectively wick away moisture from the skin surface.
- Elevations in skin pH occur when urine is mixed with stools (especially diarrhea), predisposing to breakdown of the epidermal barrier.
- Patients may have an underlying skin disorder, such as psoriasis or seborrheic dermatitis, that predisposes to skin breakdown and secondary candida infection.
- Irritant diaper dermatitis is the most common predisposing factor.

Skin Findings

- Pink to red papules coalesce into plaques with a scant amount of white scale, especially involving the inguinal creases and the gluteal cleft.
- Satellite pustules are the hallmark of candida diaper dermatitis.
- Patients may have a primary skin disorder, such as psoriasis or seborrheic dermatitis, that becomes secondarily infected with candida.
- Chronic, poorly treated candida diaper dermatitis can form granulomatous nodules (granuloma gluteale infantum).
- Candida dermatitis may produce psoriasis-like eruption at distant sites, such as the cheeks and torso.

Laboratory

- Usually laboratory testing is not necessary.
- For poorly responsive patients, consider skin biopsy, bacterial and viral cultures.

Fig. 9.5 Candidiasis (diaper dermatitis). Intense erythema under the entire diaper area. Disease may progress to this extent if topical steroids are the only treatment. Psoriasis would be in the differential diagnosis for this patient.

Fig. 9.6 Candidiasis (diaper dermatitis). Diaper dermatitis is often treated with steroid combination creams. The cortisone component may alter the clinical presentation and prolong the disease.

Differential Diagnosis

- Irritant contact dermatitis
- Psoriasis
- Seborrheic dermatitis
- Impetigo: *Streptococcus* and *Staphylococcus* species
- Cystic fibrosis
- Langerhans' cell histiocytosis
- Nutritional deficiency (e.g., zinc, biotin)

Treatment

- Therapy should be directed at minimizing wetness in the diaper area, restoring the skin barrier, and treating candida infection.
- Treat coexisting skin disease, such as seborrhea and bacterial infection.
- Frequent diaper changes and brief diaper-free periods should be encouraged.
- Barrier ointments, such as petrolatum, Aquaphor ointment, and zinc oxide ointment, restore and maintain the skin barrier.
- Commercial wet wipes may cause allergic contact dermatitis owing to fragrances and preservatives.
- Topical nystatin or econazole should be applied two to three times per day.
- Oral fluconazole weekly for 3 weeks may be required for difficult-to-treat cases.

Pearls

- Encourage parents using cloth diapers to switch to disposable diapers while the patient has dermatitis.
- Think of psoriasis and seborrheic dermatitis when diaper dermatitis fails to respond to antiyeast therapy.

Fig. 9.7 Candidiasis (diaper dermatitis). An artificial intertriginous area is created under a wet diaper, predisposing the area to a yeast infection with the characteristic red base and satellite pustules.

Fig. 9.8 Diaper candidiasis. This infant may require oral fluconazole to eradicate this candidal infection.

Candidiasis of Large Skinfolds (Candida Intertrigo)

Description

- Pink to red maceration, occurring where two skinfolds come together.
- Warm moist environment leads to disruption of the skin barrier, predisposing to yeast infection.

History

- Predisposing factors include obesity, immunodeficiency (e.g., diabetes, prednisone), hot humid weather, poor hygiene, tight-fitting clothing, and use of topical steroids.

Skin Findings

- Red moist, glistening plaques with satellite pustules and papules with a fringe of white scale.
- Painful fissures frequently occur deep within the skinfolds.

Laboratory

- Potassium hydroxide wet mount preparation from a pustule or scaly border shows spores and pseudohyphae.
- Skin biopsy and a surface culture may be necessary in treatment-resistant cases.

Course and Prognosis

- Candida intertrigo usually recurs if the underlying conditions are not corrected.

Differential Diagnosis

- Inverse psoriasis
- Seborrheic dermatitis
- Erythrasma
- Streptococcal infection
- Irritant contact dermatitis

Treatment

- Apply wet dressings (tap water or Burow's solution [aluminum acetate 1:40 solution]) with a soft cotton cloth for 20 minutes several times per day to soothe and dry the area.
- Application of an antiyeast cream (e.g., nystatin) or an antifungal (e.g., econazole) cream should be applied twice daily in a thin layer.
- Oral antifungal agents (e.g., fluconazole 100–200 mg per day for 1 week) treat resistant or severe cases.
- Sealing in the skin with a light moisturizer (e.g., Vanicream Lite or Lubriderm) may prevent recurrences by decreasing friction and acting as a protective barrier.
- Powders may be helpful to wick away moisture but may clump if there is excessive moisture.
- Patients should be encouraged to lose weight and avoid tight-fitting clothing.

Pearls

- Nystatin is not effective for dermatophyte infections, and griseofulvin and terbinafine are not effective for yeast infections.
- Consider streptococcal infection if the rash is painful and malodorous.
- Topical corticosteroid use may predispose to yeast and dermatophyte infection.
- Patients who do not respond to antiyeast medications may have inverse psoriasis.

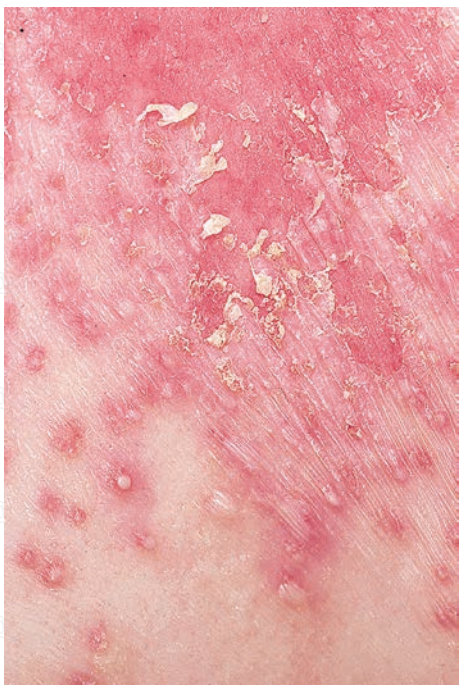

Fig. 9.9 Candidiasis under the breast. This patient shows the characteristic satellite pustules seen in candidal infections.

Fig. 9.10 Vaginal candidiasis. Red inflamed vulva and vagina with milky discharge is the hallmark of vaginal candidiasis.

Fig. 9.11 Vulvar and vaginal candidiasis. Redness without discharge may occur with vaginal candidiasis.

Fig. 9.12 Oral candidiasis. This patient with a thickened red tongue had oral candidiasis.

Fig. 9.13 Candida balanitis. Candida balanitis is itchy and painful and responds to oral fluconazole.

Fig. 9.14 Candida infection. Topical antifungal medicine should eradicate this candidal infection. Patients should seal in the skin with an emollient to prevent recurrence.

Fig. 9.15 Candida intertrigo. Cool compresses followed by topical antifungal should adequately treat candida intertrigo. Decreasing friction and moisture and application of a light emollient prevent recurrence.

Fig. 9.16 Candidiasis of large skinfolds. Skinfolds contain heat and moisture, providing an environment well suited for yeast infection. Yeast infection is made more likely with hot, humid weather, with tight or abrasive underclothing, with poor hygiene, or with inflammatory diseases occurring in the skinfolds, such as psoriasis.

Fig. 9.17 Candidiasis of large skinfolds. Pustules form, but become macerated under apposing skin surfaces and develop into groups of red papules with a fringe of moist scale at the border. Intact pustules may be found outside the apposing skin surfaces.

Fig. 9.18 Candidiasis of large skinfolds. A shallow to deep fissure is commonly found in candidal intertrigo. Intermittent use of a group VII topical steroid is effective. Powder may absorb moisture. A cool wet dressing dries the area and encourages healing.

Fig. 9.19 Candidiasis of large skinfolds. Intertrigo in the groin is common especially in obese individuals. The warm, moist apposing surfaces become red and sore. Yeast infection with papules and pustules may follow. Fungal infections usually do not cause inflammation on symmetric apposing surfaces.

Fig. 9.20 Candidiasis. A fringe of moist scale is present at the border. A red, moist, glistening plaque extends to the limits of the opposing thigh and scrotum. Compare this to tinea of the groin.

Fig. 9.21 Candidiasis. Papules and pustules are found outside the apposing skin surfaces. A red plaque extends to the border of all apposing skinfolds.

Tinea Versicolor

Description

- Tinea versicolor (caused by *Malassezia furfur*) is a common skin condition characterized by superficial scaly papules and circular plaques of varying color (white, pink, brown) on the chest, back, and shoulders.

History

- Tinea versicolor is more common in adolescents and young adults who live in warm tropical climates.
- Patients with white patches are often concerned that they are developing vitiligo.
- Patients who sweat heavily are more commonly affected.

Skin Findings

- Broad-based, rounded patches and plaques with white, powdery scale occur on the trunk and upper arms.
- Facial involvement is rare but is more likely to occur in darker individuals.
- Wood's lamp evaluation shows hypopigmentation, not depigmentation.
- Tanning of the skin often yields striking hypopigmentation.

Nonskin Findings

- Patients are healthy, although systemic disease, such as nutritional deficiency or immunosuppression, may lead to tinea versicolor.

Laboratory

- Potassium hydroxide examination shows numerous short, rod-shaped hyphae intermixed with round spores giving the "spaghetti and meatballs" pattern.

Differential Diagnosis

- Vitiligo
- Postinflammatory hypopigmentation
- Pityriasis rosea
- Nummular eczema
- Guttate psoriasis
- Hypopigmented cutaneous T-cell lymphoma

Course and Prognosis

- After successful treatment, recurrences occur in most patients. Pigmentation abnormalities persist for several weeks, despite elimination of scaling.

Treatment

- Topical selenium sulfide lotion, ketoconazole cream, econazole cream, miconazole cream, and zinc pyrithione are effective topical treatments.
- Selenium sulfide lotion 2.5% should be washed off in 20 minutes and repeated daily for 7 days and then as needed.
- Ketoconazole 2% shampoo (applied to damp skin for 5 minutes before rinsing) should be applied for at least 3 days and then as needed.
- Zinc pyrithione soap (ZNP bar) should be left on the skin for 5 minutes before rinsing.
- Fluconazole 300 to 400 mg weekly for 3 weeks is an effective treatment. To increase efficacy, patients should exercise, sweat, and shower 12 hours later. Fluconazole is concentrated in the sweat.
- Itraconazole 200 mg daily for 5 to 7 days is an effective treatment.

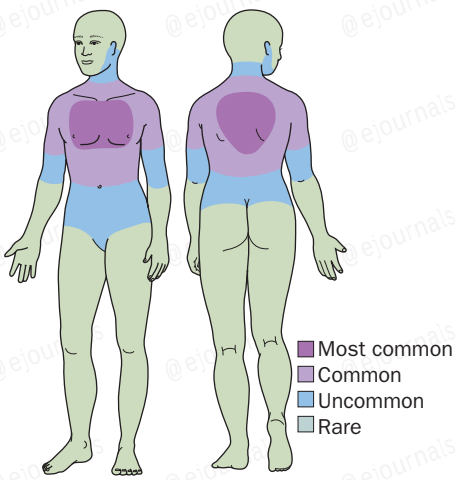

Fig. 9.22 Tinea versicolor distribution diagram.

Pearls

- Patients with recurrent tinea versicolor should consider treatment before the summer months, even in the absence of rash.
- Terbinafine (Lamisil) is not effective against *M. furfur.*
- Patients should moisturize the skin after shampooing the skin with ketoconazole, zinc pyrithione, or selenium sulfide because these agents may be drying.

Fig. 9.23 Tinea versicolor. An extensive eruption in a dark-skinned person. Lesions are lighter than normal skin. They become accentuated when uninfected skin tans. Demonstration of the fine scale helps differentiate this from vitiligo.

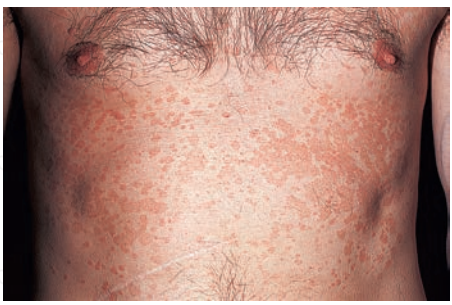

Fig. 9.24 Tinea versicolor. Lesions begin as multiple small circular macules in various colors (white, pink, brown) that enlarge radially. The lesions may be inconspicuous in fair-complexioned individuals during the winter.

Fig. 9.25 Tinea versicolor varies in extent. Some patients have a few lesions that may resemble vitiligo, pityriasis alba, or ringworm (tinea corporis). This patient had no involvement of the chest and was not aware of the infection.

Fig. 9.26 Classic presentation of tinea versicolor with white, oval, or circular patches on tan skin.

Fig. 9.27 Tinea versicolor. Lesions may be hyperpigmented or hypopigmented in African American people. The color is uniform in each individual. The lesions may be inconspicuous in fair-complexioned people during the winter.

Fig. 9.28 Tinea versicolor. A powdery scale that may not be obvious on inspection can easily be demonstrated by scraping lightly with a #15 surgical blade.

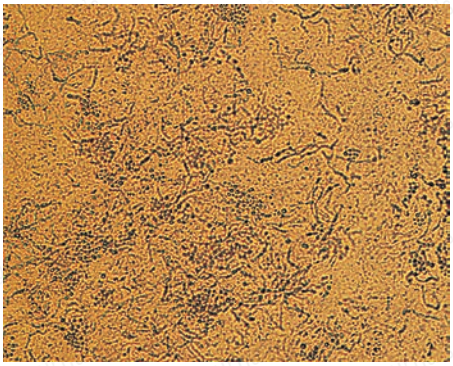

Fig. 9.29 Tinea versicolor. A potassium hydroxide wet mount. A low-power view shows numerous, short, broad hyphae and clusters of budding cells, which have been described as having the appearance of "spaghetti and meatballs."

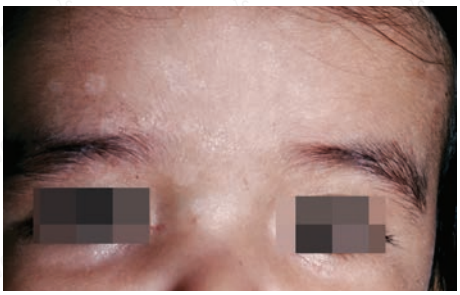

Fig. 9.30 Tinea versicolor is less common on the face, but should be considered. A potassium hydroxide wet mount preparation distinguishes tinea versicolor from pityriasis alba.

Fig. 9.31 Tinea versicolor. Dark skin does not show erythema, making inflammation difficult to see.

Malassezia Folliculitis

Description

- *Malassezia* folliculitis is a papulopustular eruption on the upper torso, caused by *M. furfur.*

History

- *Malassezia* folliculitis occurs in adolescents and young adults with a history of increased sweating.
- Diabetes mellitus, systemic chemotherapy, broad-spectrum antibiotics, and corticosteroids are predisposing factors.

Skin Findings

- *Malassezia* folliculitis produces dome-shaped monomorphic papules and pustules on the upper torso and upper arms.
- Cysts and nodules may occur in susceptible individuals.

Laboratory

- Potassium hydroxide examination shows abundant round spores and, less commonly, short hyphae.
- Skin biopsy is rarely needed but should be considered in treatment-resistant cases.
- Bacterial culture should be done when patients fail antiyeast treatment.

Differential Diagnosis

- Acne
- Bacterial folliculitis, including *Staphylococcus* and *Pseudomonas* species
- Eosinophilic folliculitis

Course and Prognosis

- Facial involvement is more persistent, is more likely to recur, and requires persistent suppression with topical antiyeast medications.
- Intermittent use of topical and oral antifungal agents may be required to control *Malassezia* folliculitis.
- Oral antibiotics may flare *Malassezia* folliculitis.

Treatment

- Selenium sulfide shampoo (Selsun) is applied and showered off 20 minutes later; this is repeated each day for 3 days to clear and then once each week for maintenance.
- Zinc pyrithione soap (ZNP bar) in the shower is also effective.
- Topical antifungal agents (e.g., ciclopirox gel or cream, econazole cream) applied nightly for 7 days is effective but may need to be repeated weekly for several months.
- A combination of oral and topical therapy is the most effective treatment. Combined ketoconazole shampoo and itraconazole (Sporanox) 200 mg for 5 days is effective.

Pearls

- *Malassezia* folliculitis of the forehead may be confused for treatment-resistant acne.
- The papules may persist for 3 to 4 weeks despite successful treatment.
- *Malassezia* folliculitis should be considered in young and middle-aged adults with itching and follicular lesions located on the trunk.

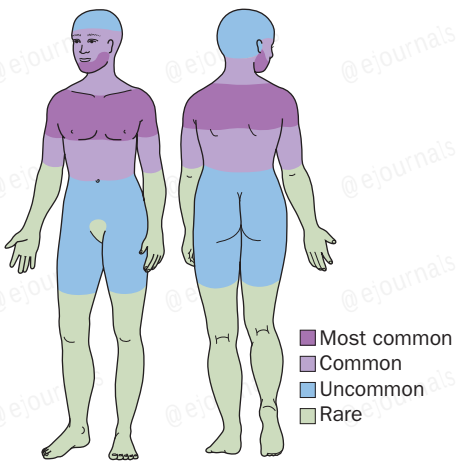

Fig. 9.32 *Malassezia* folliculitis distribution diagram.

Fig. 9.33 *Malassezia* folliculitis. Monomorphic minute pustules on the upper back. This patient had been taking oral steroids for several weeks before onset of the folliculitis.

Fig. 9.34 *Malassezia* folliculitis. *Malassezia* folliculitis is more common in patients who have increased sweating and is successfully treated with benzoyl peroxide. Oral fluconazole may be necessary in some patients.

Fig. 9.35 *Malassezia* folliculitis. This infection is seen in young people and presents with papulopustules similar to those found in acne, except that there are no comedones or cysts. Lesions occur on the back, chest, upper arms, and face. A potassium hydroxide examination shows aggregates of spores.

Tinea of the Nails (Onychomycosis)

Description

- Onychomycosis is caused by yeast or dermatophyte infection of the nail or nail bed, producing several clinical variants.

History

- The prevalence increases with age, affecting 15% to 20% of 40- to 60-year-olds.
- Most patients develop lifelong infection. *Trichophyton rubrum* and *Trichophyton mentagrophytes* are responsible for most infections.
- *Aspergillus, Cephalosporium, Fusarium,* and *Scopulariopsis* species rarely cause infection.
- Trauma, especially from tight-fitting shoes, and immunosuppression (e.g., diabetes) predispose to infection.
- A large mass composed of thick nail plate and underlying debris may cause discomfort with footwear.

Skin Findings

- There are four distinct clinical patterns of infection.
- These patterns are not exclusive and may occur simultaneously in the same or in adjacent nail plates.
- Nail infection may occur simultaneously with hand or foot tinea or may occur as an isolated infection.

Distal Subungual Onychomycosis

- This is the most common pattern.
- Fungi invade the distal area of the nail bed.
- The distal plate turns yellow or white as an accumulation of debris causes the nail to rise and separate from the underlying bed.

White Superficial Onychomycosis

- *T. mentagrophytes* is the most common cause and produces surface invasion of the nail plate.
- The nail surface is soft, dry, and powdery and can easily be scraped away.
- The nail plate is not thickened and remains adherent to the nail bed.

Proximal Subungual Onychomycosis

- *T. rubrum* is the most common cause and invades under the proximal cuticle, causing the nail to separate from the proximal nail fold.
- This is the most common pattern seen in patients with human immunodeficiency virus infection.

Candida Onychomycosis

- Nail plate infection caused by *C. albicans* is seen almost exclusively in chronic mucocutaneous candidiasis. All nails are involved.
- The nail plate thickens and turns yellow to brown.

Laboratory

- Potassium hydroxide wet mount preparation is the quickest method to establish the diagnosis.
- Fungal culture of nail bed or nail plate assists in diagnosis.
- Submit nail clippings for histology (nail biopsy).

Differential Diagnosis

- Psoriasis
- Lichen planus
- Nail trauma (specially to the matrix)
- Twenty-nail dystrophy

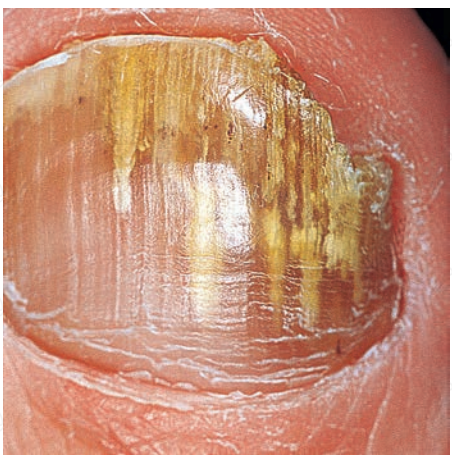

Fig. 9.36 Distal subungual onychomycosis. Various patterns are produced as the fungi grow proximally. Yellow longitudinal channels are highly characteristic of tinea.

Course and Prognosis

- Onychomycosis usually starts in one or two nails and gradually spreads to involve more nails.
- Nail disease is usually lifelong, unless treated.
- Topical treatment results in low cure rates (less than 30%).
- Systemic treatment produces higher cures rates (greater than 80%).
- Relapse occurs in 15% to 20% per year.
- Onychomycosis causes pain when the nails are thick and limit a patient's activity.
- Brittle thick nails may disrupt surrounding skin and predispose to bacterial infection of the surrounding tissues (paronychia).
- Onychomycosis is embarrassing for many patients, especially if the fingernails are involved.

Treatment

- Topical treatments include ciclopirox olamine 8%, efinaconazole 10%, and tavaborole 5%. They are a safe alternative to oral medications.
- Systemic treatments include terbinafine 250 mg daily and itraconazole 200 mg daily (6 weeks for fingernails and 12 weeks for toenails). Pulsed treatment may be used for terbinafine, itraconazole, and fluconazole. Fluconazole 300 to 400 mg weekly for 6 to 9 months is very safe and effective.
- Laser treatment for onychomycosis is costly and not very effective.

Pearls

- Removal of the nail plate results in higher cure rates and longer remissions.
- Terbinafine is not effective for yeast onychomycosis.

Fig. 9.37 Distal subungual onychomycosis. Yellow to brown color extends down one side of the nail.

Fig. 9.38 Distal subungual onychomycosis. Infection involves the entire distal plate. Hyphae have invaded the full thickness of the nail and have caused it to crumble.

Fig. 9.39 Distal subungual onychomycosis. A large mass composed of thick nail plate and underlying debris may cause discomfort with footwear.

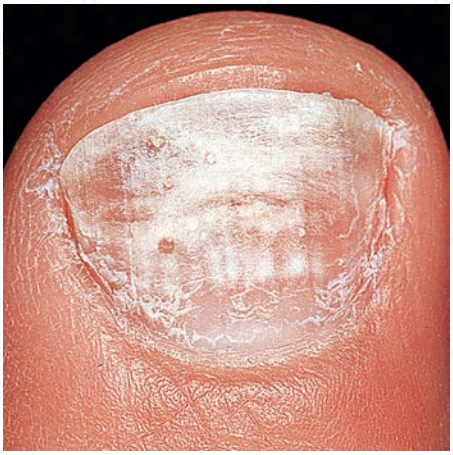

Fig. 9.40 White superficial onychomycosis. The surface of the nail is soft, dry, and powdery and can easily be scraped away. The nail plate is not thickened and remains adherent to the nail bed.

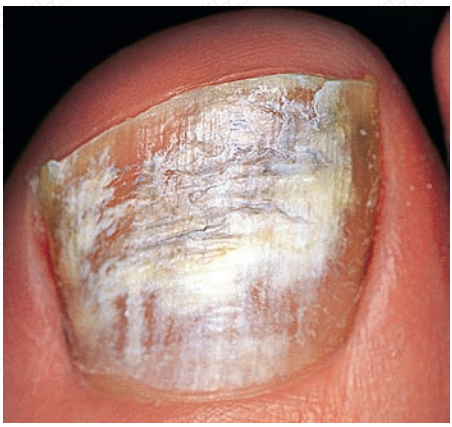

Fig. 9.41 White superficial onychomycosis. The surface of the nail plate has been invaded and is crumbling away.

Fig. 9.42 Proximal subungual onychomycosis. Microorganisms enter the cuticle area of the posterior nail fold, migrate to the underlying matrix, and finally invade the nail plate from below.

Fig. 9.43 Proximal subungual onychomycosis. Hyperkeratotic debris accumulates and causes the nail to separate. This is the most common pattern seen in patients with HIV.

Angular Cheilitis (Perlèche)

Description

- Angular cheilitis is painful redness and fissuring at the angles of the mouth. Deep skinfolds at the angles of the mouth traps saliva, causing skin breakdown, fissuring, and secondary bacterial and yeast infection.

History

- It is common in elderly patients with skin laxity, resulting in deep folds at the corners of the mouth.
- Predisposing factors include lip licking, thumb sucking, poorly fitting dentures, and dental flossing.
- Whitening toothpaste and mouthwash are irritating to the skin and may exacerbate angular cheilitis.

Skin Findings

- Redness and swelling produce painful red papules, pustules, and fissures at the corners of the mouth.
- Pustules may indicate secondary bacterial and fungal infection.

Laboratory

- Surface culture should be done for yeast and bacteria.
- Herpes simplex PCR testing should be considered if the patient has a history of herpes simplex virus.

Differential Diagnosis

- Allergic contact dermatitis
- Herpes simplex virus
- Nutritional deficiency

Course and Prognosis

- Skin breakdown quickly leads to secondary infection that produces redness and painful fissures.
- Angular cheilitis can become a recurrent chronic problem if the predisposing factors are not corrected.

Treatment

- The skin barrier should be enhanced with a petrolatum or oil-based ointment to protect against saliva.
- Secondary infection should be treated with an antiyeast cream, such as nystatin or econazole. If bacterial infection is considered, mupirocin should be added to the regimen. Low-strength corticosteroids, such as 1% hydrocortisone and desonide 0.05 %, decrease inflammation.
- Oral antifungals (fluconazole) and oral antibiotics (antistaphylococcal) may be required for severe cases.
- Rarely, injectable fillers or lasers are required to lessen skin laxity.

Fig. 9.44 Angular cheilitis. Patients lick and moisten the area in an attempt to prevent cracking. This only aggravates the problem and may lead to eczematous inflammation, staphylococcal infection, or hypertrophy of the skinfold.

Fig. 9.45 Angular cheilitis. Chronically inflamed surfaces become infected with a mixed flora of yeast and bacteria. Crust and exudate form, and the site becomes painful.

Pearls

- Avoid mixing topical therapies for convenience of application because this dilutes the concentrations of active ingredients and reduces their effectiveness.
- Inquire about dental hygiene products because many patients are inappropriately flossing their teeth and overusing teeth whitening mouthwash and toothpaste.

Fig. 9.46 Angular cheilitis. This elderly patient experiences recurrent inflammation from saliva flowing into the deep skinfold at the angle of the mouth.

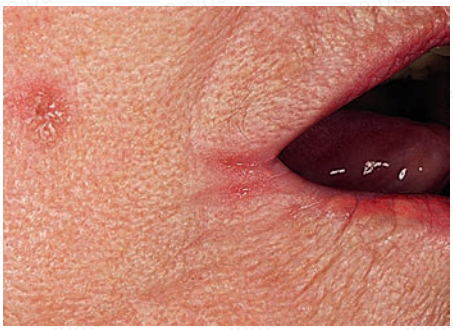

Fig. 9.47 Angular cheilitis. Fissures have formed in the valleys of the skin creases at the mouth angle. These tiny intertriginous surfaces become macerated and inflamed when constantly exposed to saliva.

Cutaneous Fungal Infections

Description

- Dermatophyte fungi (*Microsporum, Trichophyton,* and *Epidermophyton* species) infect the skin and cause red papules, pustules, and nodules that coalesce into round plaques with an advancing border and a relatively clear center.

History

- Dermatophytes originating from animals (zoophilic) and from soil (geophilic) elicit a brisk inflammatory response, resulting intense redness and pustules.
- Anthropophilic dermatophytes capable of growing only on human skin and nails elicit a mild inflammatory response, resulting in scaly skin with minimal redness.
- Dermatophyte skin infection is also called *tinea* and is named based on the affected body region (scalp—tinea capitis, beard—tinea barbae, face—tinea faciei, body—tinea corporis, hand—tinea manum, foot—tinea pedis, nails—onychomycosis) (Table 9.1).
- Predisposing factors for tinea infection include moist, macerated skin, exposure to animals (e.g., cows, dogs, kittens), affected family members (especially tinea capitis and onychomycosis), topical corticosteroid use, immunosuppressed states (e.g., diabetes, chemotherapy), and athletics (e.g., wrestlers).
- Dermatophyte infections are often insidious in onset.

Skin Findings

- Classically, dermatophyte infections elicit papules and plaques with a rounded edge and white scale.
- Dermatophytes infect hair follicles, causing pink to red papules and nodules.
- Pustules are caused by more intense inflammation (e.g., zoophilic or geophilic organisms).

Laboratory

- Potassium hydroxide wet mount should be performed from the advancing lesion edge.
- The most hyphae are obtained from the advancing border.
- Fungal cultures may be necessary (e.g., tinea capitis, tinea barbae, and Majocchi's granuloma) to confirm the diagnosis.
- Using Wood's lamp, hair, not the skin of the scalp, fluoresces with a blue to green color if infected with *Microsporum canis* or *Microsporum audouinii.*

Differential Diagnosis

- Dermatophyte infection of the face, hands, torso, extremities
  - Nummular dermatitis
  - Psoriasis
  - Impetigo
  - Tinea versicolor
- Dermatophyte infection in the intertriginous areas
  - Candida intertrigo
  - Inverse psoriasis
  - Erythrasma *(Corynebacterium minutissimum)*
  - Seborrheic dermatitis
  - Hailey–Hailey disease
- Dermatophyte infection of the hair
  - Bacterial folliculitis
  - Herpes simplex virus
  - Varicella-zoster virus
  - Psoriasis
  - Seborrheic dermatitis

Treatment

- Limited cutaneous involvement can be treated with topical agents once to twice daily for 2 to 6 weeks
  - Imidazoles (clotrimazole, econazole, miconazole, oxiconazole, sertaconazole, luliconazole, eberconazole)
  - Allyamines (terbinafine, naftifine, butenafine)
  - Ciclopirox olamine
  - Tolnaftate
  - Undecylenic acid
- Widespread cutaneous involvement or hair involvement should be treated with a systemic antifungal agent.
  - Terbinafine—cutaneous: 250 mg per day for 1 to 2 weeks; hair: same dose for 3 to 4 weeks, see table for pediatric dosing (Table 9.2).
  - Itraconazole—cutaneous: 200 mg/day or 3 to 5 mg/kg/day (maximum, 200 mg)

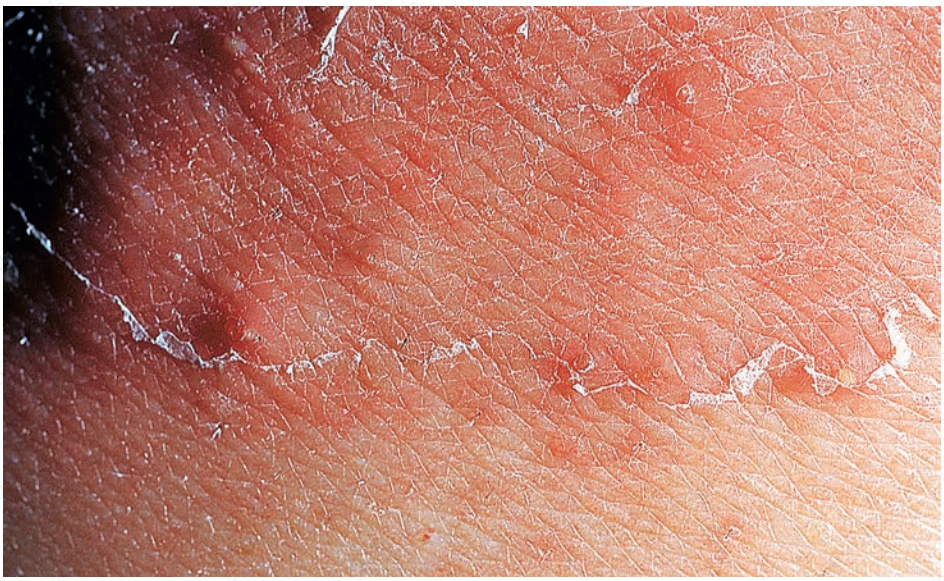

Fig. 9.48 Cutaneous fungal infections. A very characteristic pattern of inflammation is the active border of infection. The highest numbers of hyphae are located in the active border, and this is the best area to get a sample for a potassium hydroxide examination. This pattern is present in all locations except the palms and soles.

Fig. 9.49 Cutaneous fungal infections. Scale is obtained by holding a #15 surgical blade perpendicular to the skin surface and smoothly but firmly drawing the blade with several short strokes against the scale.

for 1 week; hair: 5 mg/kg/day (maximum, 400 mg in adults and 500 mg in children) for 4 to 8 weeks.

- Griseofulvin—cutaneous: 500 to 1000 mg/day (microsize) or 375 to 500 mg/day (ultramicrosize) in adults for 2 to 4 weeks and 15 to 20 mg/kg/day in children for 2 to 4 weeks; hair: 10 to 15 mg/kg/day ultramicrosize (maximum, 750 mg) in adults for 6 to 8 weeks and 20 to 25 mg/kg/day (microsize suspension) in children for 6 to 8 weeks.

Table 9.1 Unique Historical, Clinical, Diagnostic, and Treatment Differences Between Distinct Clinical Patterns of Cutaneous Dermatophyte Infection

Tinea	Historical	Clinical	Diagnostic	Treatment
Capitis	90% caused by *Trichophyton tonsurans* *Microsporum canis* from kittens Fomites important in transmission More common in African Americans and Hispanics More common in children	Four patterns: (1) Seborrheic dermatitis—most common (2) Inflammatory (kerion)—boggy scalp—may be confused with cellulitis (3) Black dot—large areas of alopecia (4) Pustular minimal scaling Posterior cervical adenopathy present	Potassium hydroxide—often negative Cultures—diagnostic May use brush culture method or cotton swab Wood's lamp positive only for *Microsporum* spp.	Kerion—may need prednisone and antistaphylococcal antibiotic Use selenium sulfide or ketoconazole shampoo to decrease fungal shedding
Faciei and corporis	More common in warm climates Epidemics in wrestlers Reinfection is common in contact sports	Patterns: (1) Annular plaques (classic) (2) Deep inflammatory—red nodules and pustules (3) Majocchi's granuloma—deep hair follicle infection	Potassium hydroxide—abundant hyphae Perform bacterial and fungal cultures	Wrestlers may need to be treated throughout season to prevent reinfection
Barbae	Slowly evolves in farmers—"barn itch" and wrestlers Usually one part of the beard Hairs are often loose and easily fall out	Starts as follicular pustules Patterns: (1) Annular pattern—*Trichophyton rubrum* and *Trichophyton violaceum* (2) Follicular pattern—*Trichophyton mentagrophytes* and *Trichophyton verrucosum*	Potassium hydroxide Bacterial and fungal culture	Topical antifungals not effective Similar treatment to tinea capitis

Manum	More common in adults Insidious onset Often associated with foot and nail infection	Patterns: (1) Annular pattern (2) Thick palm skin (3) White scale—"one hand, two feet"	Potassium hydroxide and fungal culture	Topical antifungals usually effective Must treat concurrent nail and feet disease to prevent recurrence
Pedis	Most common area infected with dermatophytes Uncommon in prepubertal children Predisposing factors: shoes, locker rooms, communal baths Atopic individuals are prone to recurrent *T. rubrum* infections	Patterns: (1) Interdigital—extend onto plantar and dorsal foot (2) Scaly—thickened skin or moccasin type (*T. rubrum*) (3) Vesicular—may be pustular—allergic response to fungus and may involve distant sites	Potassium hydroxide and fungal culture	Topical antifungals are used for at least 2 weeks after the symptoms resolve to prevent recurrence Burow's soaks for vesicular weepy lesions Severe/resistant cases—oral antifungal for 2–4 weeks "Id reactions" may require topical corticosteroid and in severe cases a systemic corticosteroid
Cruris	More common in postpubertal males Predisposing factors: sweating, concurrent skin, or nail infection	Half-moon red plaques with advancing scale and pink-red papules and pustules in the groin Scrotum rarely involved	Potassium hydroxide and fungal culture	Topical antifungals with activity against yeast and dermatophytes (e.g., econazole, miconazole, clotrimazole) Oral antifungal for severe or resistant cases Avoid combination antifungal creams—may cause skin thinning

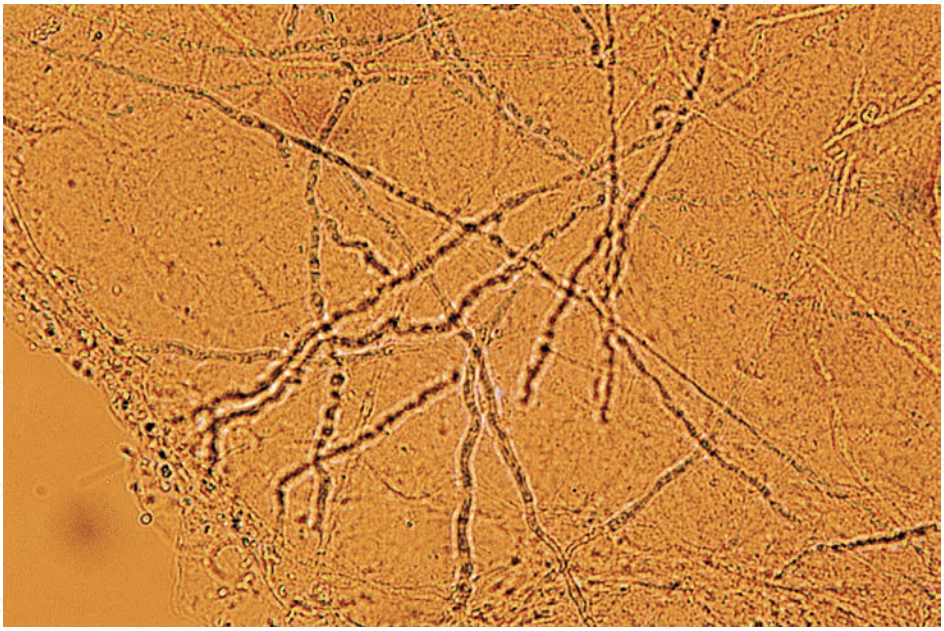

Fig. 9.50 Cutaneous fungal infections. Dermatophytes appear as translucent, branching, rod-shaped filaments (hyphae) of uniform width, with lines of separation (septa) spanning the width and appearing at irregular intervals.

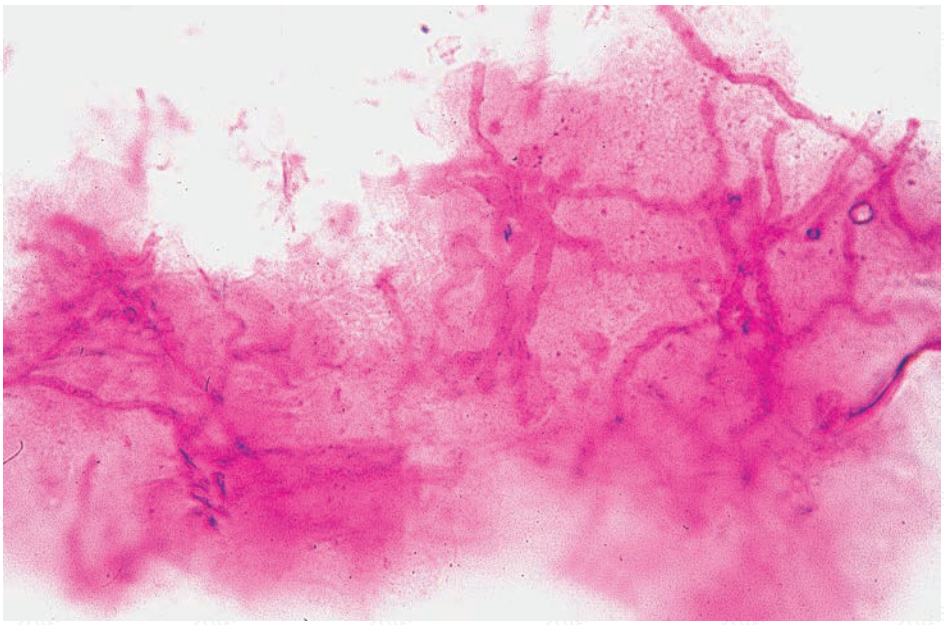

Fig. 9.51 Cutaneous fungal infections. Hyphae may be difficult to find in a potassium hydroxide wet mount. Parker's blue ink and other stains easily stain the hyphae, rendering them visible under low power.

Table 9.2 Daily Dosage of Terbinafine

Body Weight	Daily Dose
Less than 20 kg (44 lb)	62.5 mg (¼ tablet)
20–40 kg (44–88 lb)	125 mg (½ tablet)
More than 40 kg (88 lb)	250 mg (1 tablet)

- Fluconazole—cutaneous: 6 mg/kg/week (maximum, 200 mg) for 2 to 4 weeks; hair: same dose for 3 to 6 weeks.

Pearls

- Tinea pedis may require longer durations of treatment with topical and systemic agent.
- Tinea incognito is a localized cutaneous fungal infection, the appearance of which has been altered by application of topical corticosteroids.
- Tinea amiantacea, a form of seborrheic dermatitis that occurs in children, is frequently misdiagnosed as tinea capitis.
- Cotton culturette is an effective method to culture in children.
- Tinea treated with topical steroids will flourish and develop multiple rings and pustules and is referred to as *tinea incognito*.

Fig. 9.52 Interdigital tinea pedis (toe web infection). Tight-fitting shoes compress the toes, creating a warm and moist environment in the toe webs; this environment is suited to fungal growth.

Pediatric Considerations

- Inflammatory tinea capitis (kerion) mimics cellulitis. Children with large, weepy plaques should be cultured and treated for fungal infection in addition to bacterial infection.
- Infants with chronic diaper rashes not responding to standard measures should be sent to a specialist to evaluate for underlying histiocytosis or nutritional deficiency, such as acrodermatitis enteropathica.
- Children with kittens are at risk for inflammatory tinea infections. Avoid steroid and antifungal combination drugs.

Fig. 9.53 Interdigital tinea pedis (toe web infection). The web can become dry, scaly, and fissured or white, macerated, and soggy.

Fig. 9.55 Tinea of the foot. Interdigital involvement extending onto the dorsal foot. Potassium hydroxide examination will discern tinea from eczema.

Fig. 9.54 Tinea of the foot. Tinea of the soles often presents with a dry, scaling surface. The entire sole of one or both feet may be involved. It is sometimes difficult to demonstrate hyphae in a potassium hydroxide preparation. The infection is difficult to treat with topical medication.

Fig. 9.56 Tinea of the foot. Classic ringworm pattern of fungal infection.

Fig. 9.57 Tinea of the foot. Erythema and scale extend onto the sides of the foot. This pattern resembles eczema.

Fig. 9.58 Tinea of the foot. The typical pattern is to see infection of two hands and one foot, or two feet and one hand. Both palms and soles show involvement of the entire surface and resemble dry skin.

Fig. 9.59 Pitted keratolysis. Longitudinal furrows and pits are classic for pitted keratolysis. Pitted keratolysis is caused by bacteria that thrive in moist environments.

Fig. 9.60 Tinea pedis. This patient developed an itchy blistering eruption on the soles of both feet due to a dermatophyte infection.

Fig. 9.61 Onychomycosis and tinea pedis. Patients with onychomycosis are at risk for tinea pedis. Tinea pedis may predispose to cellulitis, especially in patients with diabetes.

Fig. 9.62 Tinea of the groin. A half-moon–shaped plaque forms with well-defined scaling, and sometimes a vesicular border advances out of the crural fold onto the thigh. The skin within the border turns red-brown, is less scaly, and may develop red papules.

Fig. 9.63 Tinea of the groin. The entire surface of this lesion is dry and scaling. Involvement of the scrotum is unusual, as opposed to *Candida* species infections in which it is common.

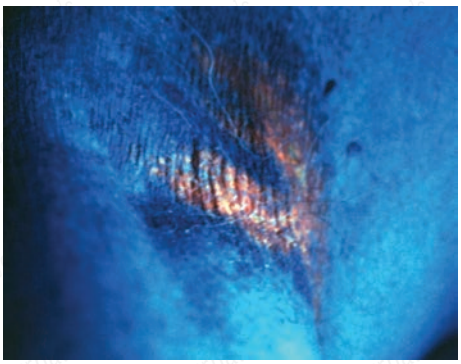

Fig. 9.64 Erythrasma. Pink rashes with superficial scale should be checked with a Wood's lamp because *Corynebacterium minutissimum* infection can appear similar to candidal intertrigo. Erythrasma shows a coral red fluorescence on Wood's lamp evaluation. Satellite pustules are seen in candidal intertrigo, but not erythrasma.

Fig. 9.65 Tinea of the groin. The ringworm pattern of infection may also appear in the groin.

Fig. 9.66 Tinea of the groin. The ringworm pattern of infection with multiple round superficial plaques with scaling borders. Lesions are present on the thighs and up to the lateral aspect of the scrotum.

Fig. 9.67 Tinea of the body. Inflammatory lesions. In classic ringworm, lesions begin as flat, scaly spots that develop a raised border that extends out at variable rates in all directions. The advancing scaly border may have red, raised papules or vesicles.

Fig. 9.68 Tinea of the body. Round annular lesions. Larger lesions tend to be mildly itchy or asymptomatic. They may reach a certain size and remain for years with no tendency to resolve.

Fig. 9.69 Tinea of the body. Tinea may be asymptomatic or itchy. Infection can be subtle and present for years. Very large areas may be infected.

Fig. 9.70 Tinea incognito. A diagnosis of psoriasis was incorrectly made months ago. Repeated treatment with the group I topical steroid clobetasol caused this widespread infection.

Fig. 9.71 Tinea of the body. Large geographic plaque on the back with typical raised, scaling border.

Fig. 9.72 Tinea of the body. Buttock involvement usually extends from groin involvement (tinea cruris).

Fig. 9.73 Tinea of the body. Note the annular pattern with advancing scaling border.

Fig. 9.74 Tinea of the body. Plaques covering a wide area appear to be eczema. The papules and pustules represent invasion of infection deep into the hair follicles. Topical antifungal medications may not penetrate deep enough to be effective.

Fig. 9.75 Tinea of the face. Tinea can occur on the face and look like eczema, psoriasis, or seborrheic dermatitis. Application of topical steroids will result in a widespread bizarre pattern of infection.

Fig. 9.76 Tinea of the body. Round annular lesions. The border and central area are papular and vesicular.

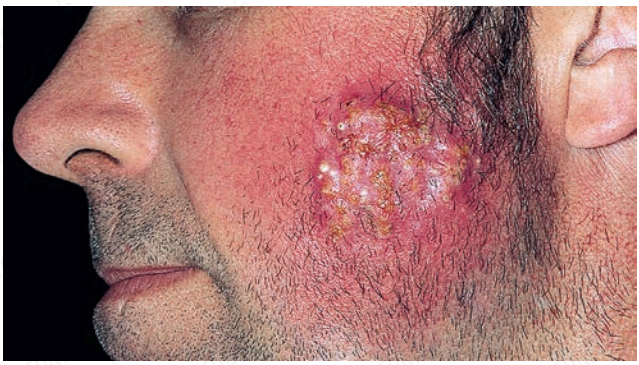

Fig. 9.77 *Trichophyton verrucosum.* "Barn itch" is seen in famers who rest their head against an infected cow while milking. Fungal infections caught from cows are highly inflammatory.

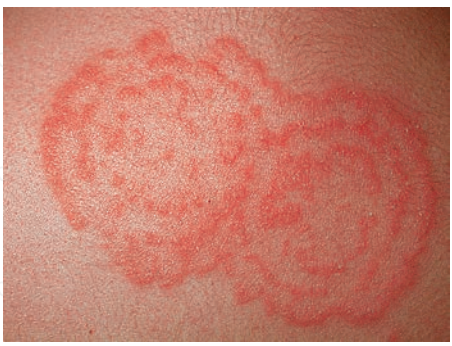

Fig. 9.78 Tinea of the body. The classic ringworm pattern of infection. This patient had been treated with triamcinolone, which resulted in the concentric rings.

Fig. 9.79 Tinea of the body. The ringworm pattern of infection is highly characteristic.

Fig. 9.80 Tinea of the face. Ringworm of the face is not common. It is often misdiagnosed as eczema or seborrheic dermatitis. Look for the sharp, scaling border.

Fig. 9.81 Tinea incognito. Fungal infections treated with topical steroids often lose some of their characteristic features. Diffuse erythema, diffuse scale, scattered pustules or papules, and brown hyperpigmentation may all result.

Fig. 9.82 Tinea of the body. This large plaque was diagnosed as psoriasis. However, it lacks the silvery surface scale seen in psoriatic plaques. The scaling border is the diagnostic feature.

Fig. 9.83 Tinea corporis. This child had a kitten and developed this inflammatory tinea corporis. Inflammatory tinea should be distinguished from nummular dermatitis and impetigo with a potassium hydroxide wet mount.

Fig. 9.84 Pitted keratolysis is often confused for tinea pedis. The feet are malodorous and slimy. Patients should be treated with Drysol and topical erythromycin.

Fig. 9.85 Tinea of the dorsal aspect of the hand (tinea manuum) has all of the features of tinea corporis. The nails are also frequently infected.

Fig. 9.86 Tinea of the palms has the same appearance as the dry, diffuse, keratotic form of tinea on the soles. It may be asymptomatic, and the patient may be unaware of the infection, attributing the dry, thick, scaly surface to hard physical labor.

Fig. 9.87 Tinea incognito. Fungal infections treated with topical steroids often lose some of their characteristic features. Multiple rings have appeared.

Fig. 9.88 Tinea of the hand. Ringworm pattern of infection. Lesions had been present for months. They responded to topical antifungal creams.

Fig. 9.89 Tinea incognito. Fungal infections treated with topical steroids can lose some of their characteristic features. Here, a once localized process has expanded greatly.

Fig. 9.90 Tinea incognito. Note the annular pattern with advancing scaling border.

Fig. 9.91 Tinea incognito. Topical steroid creams modify the typical clinical presentation of tinea. Red papules sometimes appear at the edges and center of the lesions. This modified form may not be immediately recognized as tinea.

Fig. 9.92 Tinea incognito. The eruption may be much more extensive, and the advancing scaly border may not be present.

Fig. 9.93 Tinea incognito. Diffuse erythema, diffuse scaling, scattered pustules or papules, and brown hyperpigmentation may all result. All of the characteristic features of tinea have been lost.

Fig. 9.94 Tinea of the scalp with many round areas of scale and alopecia. Wood's light examination showed green hairs. *Microsporum canis* from a pet cat grew in the culture.

Fig. 9.95 Inflammatory tinea capitis (kerion). There is an inflamed, boggy, tender area of alopecia with pustules. Occipital adenopathy was present.

Fig. 9.96 Inflammatory tinea capitis caused by *Trichophyton tonsurans*. Permanent hair loss occurred after this destructive infection.

Fig. 9.97 Tinea of the scalp. Scale and pustules may be seen. A once chronic infection can become inflammatory.

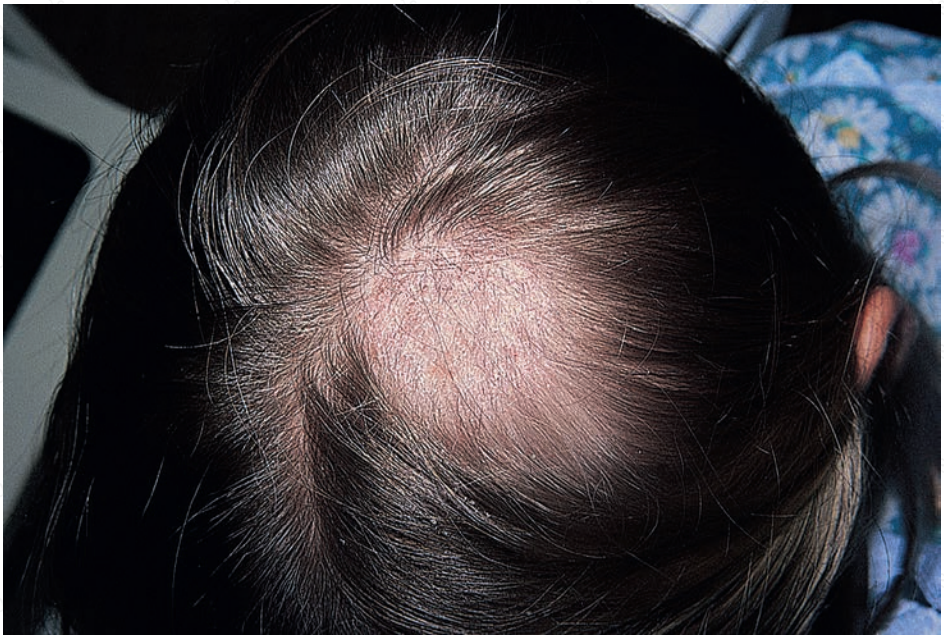

Fig. 9.98 Tinea of the scalp. Noninflammatory lesions tend to be chronic and last for months. Hairs break off at or below the scalp surface, resulting in a "black dot" appearance of the scalp surface.

Fig. 9.99 Tinea of the beard. Tinea begins insidiously with a small group of follicular pustules. The process becomes confluent and resembles bacterial infection or seborrheic dermatitis. Potassium hydroxide examination proves the diagnosis.

Fig. 9.100 Tinea of the beard. Superficial infection. This pattern resembles the annular lesions of tinea corporis. The hair is usually infected.

Fig. 9.101 Tinea of the beard. Deep follicular infection. This pattern clinically resembles bacterial folliculitis except that it is slower to evolve and is usually restricted to one area of the beard. Look carefully for the well-defined, sharp, advancing border.

Fig. 9.102 Tinea of the beard. Secondary staphylococcal infection may occur with tinea capitis and tinea of the beard. Tinea must be considered in patients with intense inflammatory rashes in the hair-bearing areas.

Fig. 9.103 *Trichophyton tonsurans*. Black-dot tinea capitis produces alopecia without inflammation or scarring.

Fig. 9.104 *Trichophyton tonsurans*. Light hair will produce alopecia with white dots.

10 Exanthems and Drug Reactions

James G. H. Dinulos

Nonspecific Viral Rash

Description

- An exanthem is a rash that occurs as a sign of a systemic disease. A viral exanthem is a rash that arises because of a viral infection.
- Most viruses produce similar rashes, leading to the term *nonspecific viral rash*.

History

- Nonspecific viral rashes are the most common viral exanthems and are challenging to diagnose.
- Historic elements such as season, exposure history, and local and regional epidemiology are important in the evaluation of a patient with a suspected viral exanthem.
- Most nonspecific viral exanthems in the winter are due to respiratory viruses; in the summer and fall they are due to the enteroviruses.
- Examples of viruses capable of causing nonspecific viral exanthems include nonpolio enteroviruses (enterovirus, coxsackievirus, echovirus), Epstein–Barr virus, human herpesvirus 6, human herpesvirus 7, parvovirus B19, and respiratory viruses (rhinovirus, adenovirus, parainfluenza virus, respiratory syncytial virus, influenza virus).

Skin Findings

- Nonpolio enterovirus can produce generalized erythematous macules and papules.
- Sometimes these viruses produce petechial rashes that can mimic meningococcemia.
- Epstein–Barr virus causes pharyngitis, morbilliform (5%–15%), vesicular, urticarial, and petechial rashes. Periorbital edema occurs in 35% of patients with this virus.
- All respiratory viruses can cause diffuse pink macules and papules that coalesce to plaques. Many patients with adenovirus infection develop keratoconjunctivitis that is highly contagious.
- Papular acrodermatitis of childhood (Gianotti–Crosti syndrome) is a viral exanthem characterized by monomorphic, discrete papules and vesicles coalescing on the face, extremities, and buttocks.
- Unilateral laterothoracic exanthem (asymmetric periflexural exanthem) is a rash occurring on the lateral thorax, near the axilla. Sometimes this viral exanthem will spread to the other hemithorax and the extremities.
- Papular–purpuric gloves and socks syndrome is an acute self-limiting rash characterized by petechial erythema on the palms and soles. Patients with this may have fevers and flu-like symptoms. Most cases are caused by parvovirus B19.
- Severe coxsackievirus A6 may cause erosive vesicles and bullae mimicking widespread herpes simplex infection ("eczema coxsackium").

Nonskin Findings

- Nonskin findings vary according to the specific virus. Most nonspecific viruses are associated with fever and constitutional symptoms.
- Nonpolio enteroviruses cause fever, abdominal pain, and vomiting. There can be multiorgan involvement, including the central nervous system and the pulmonary and cardiac systems. These viruses can mimic serious bacterial illness.
- Epstein–Barr virus can produce fever, sore throat, lymphadenopathy, abdominal pain, myalgias, and hepatosplenomegaly.

Laboratory and Biopsy

- The laboratory evaluation should be focused and directed by the history and physical examination.

- Skin biopsy findings are not specific but can be helpful to distinguish between staphylococcal scalded skin syndrome and drug hypersensitivity reaction.

Differential Diagnosis

- Drug hypersensitivity reaction
- Kawasaki disease
- Staphylococcal scalded skin syndrome
- Toxin-mediated erythema (toxic shock syndrome, staphylococcal toxic shock syndrome)

Course and Prognosis

- Most nonspecific viral exanthems are self-limited and resolve in 1 to 2 weeks.
- The rash of Gianotti–Crosti syndrome can last up to 8 weeks.

Fig. 10.1 Nonspecific viral rash. Viral exanthems and drug rashes may have the same appearance. They are symmetric and widespread.

Pediatric Considerations

- Viral exanthems are common in childhood and can be difficult to distinguish from morbilliform drug reactions.
- Measles vaccination exanthem occurs in 5% of those receiving the vaccine.
- Kawasaki disease should be considered in small infants with exanthems and prolonged fever.

Fig. 10.2 Nonspecific viral rash. Viral exanthems may have different presentations. This symmetric maculopapular eruption appeared suddenly with other viral symptoms. Oral medications had not been used.

Fig. 10.3 Nonspecific viral rash. This symmetric eruption of sudden onset produces only mild itching. It resolved in 2 weeks without any treatment.

Fig. 10.4 Nonspecific viral rash. Generalized nonpruritic erythematous papules are also referred to as a *morbilliform* or *measles-like rash*.

Roseola Infantum

Description

- Roseola infantum is a viral exanthem characterized by high fever followed by the abrupt appearance of a diffuse rash as the fever resolves.

History

- Roseola infantum occurs in infants from the ages of 6 months to 3 years, with a peak incidence at 6 months.
- It is caused by human herpesvirus 6 and human herpesvirus 7.
- Most cases occur during early spring, although roseola infantum can occur anytime during the year.
- The incubation period is 12 days (range, 5–15 days).
- Infants appear well, except for a high fever (38.3°–41.1° C).

Skin Findings

- Within 2 days of defervescence, small, pink, almond-shaped macules occur on the neck, trunk, proximal extremities, and face.
- The rash is not itchy and fades within several days to a week.
- Eyelid edema is seen in 30% of children.
- Most patients have pink papules on the uvula and soft palate.

Nonskin Findings

- Irritability can occur in up to 14% of patients.
- Posterior cervical, occipital, and posterior auricular adenopathy are common.
- Open fontanels are sometimes bulging.
- Complications include febrile seizures, aseptic meningitis, hemiplegia, and encephalitis or encephalopathy.

Laboratory and Biopsy

- Leukocytosis develops at the onset of fever.
- Leukopenia with a granulocytopenia and relative lymphocytosis appears as the temperature increases and persists until the eruption fades.
- Serologic testing is available, but typically is not helpful.
- Skin biopsy findings are not specific.

Differential Diagnosis

- Other viral exanthems (e.g., parainfluenza virus, parvovirus B19, rubella, enterovirus)
- Drug eruptions

Course and Prognosis

- Prodromal symptoms include a sudden onset of high fever of 39.4° to 41.1° C.
- Most children appear to be inappropriately well, given the high fever.
- Roseola is a major cause of visits to the emergency department, of febrile seizures, and of hospitalizations.

Treatment

- Acetaminophen and ibuprofen are effective antipyretics.
- Immunocompromised hosts or children with a severe illness may require antiviral treatment (valganciclovir, ganciclovir, cidofovir, foscarnet).

Pearls

- Infections by herpesvirus types 6 and 7 should be suspected in infants with febrile convulsions—even those without the exanthem.
- People with AIDS can have disseminated multisystem involvement, and transplant recipients can have reactivation of latent virus.

Fig. 10.5 Roseola infantum. Numerous pale-pink, almond-shaped macules.

Fig. 10.6 Roseola infantum. Pale-pink macules may first appear on the neck.

Erythema Infectiosum (Fifth Disease)

Description

- Erythema infectiosum, also known as *fifth disease* or *slapped cheek disease*, is a common viral exanthem that causes bright-red cheeks and lacy erythema of the arms.

History

- Erythema infectiosum occurs in the winter and spring and is associated with community outbreaks.
- It is caused by parvovirus B19 and is transmitted through respiratory secretions or blood, or vertically from mother to fetus.
- Peak attack rates occur in children aged 5 to 14 years.
- During outbreaks, 60% of susceptible schoolchildren and 30% of susceptible adults acquire the infection.
- Asymptomatic infection is common.
- The incubation period is 4 to 14 days.
- Prodromal symptoms are usually mild or absent. Pruritus, low-grade fever, malaise, and sore throat precede the eruption in approximately 10% of cases. Lymphadenopathy is absent. Older persons may complain of joint pain.

Skin Findings

- There is facial erythema—the slapped cheek appearance. Red papules on the cheeks rapidly coalesce in hours, forming red, slightly edematous, warm, erysipelas-like plaques that are symmetric on both cheeks and spare the nasolabial fold and the circumoral region (circumoral pallor). The slapped cheek appearance fades in 4 days.
- Approximately 2 days after the slapped cheek rash, lacy erythema in a "fish net" pattern begins on the proximal extremities and extends to the trunk and buttocks, fading in 6 to 14 days.
- For the next 2 to 3 weeks, the eruption fades and reappears in previously affected sites. Factors such as sunlight, hot water, and physical and emotional exertion exacerbate the rash.
- The rash fades without scaling or pigmentation, and the palms and soles are spared.

Nonskin Findings

Adults

- Women may develop itching and arthritis. The itching varies from mild to intense and is localized or generalized.
- Women tend to develop a moderate to severe, symmetric migratory polyarthritis (especially the small joints of the hands and knees), similar to rheumatoid arthritis. The duration of the arthritis is variable, lasting from 2 weeks to 4 years.
- Generally, men do not develop arthritis.
- The arthritis is preceded by a nonspecific macular eruption, unlike the typical lacy rash.
- Flu-like symptoms and joint pains coincide with immunoglobulin G antibody production (18–24 days after exposure), suggesting that immune complexes play an important role in extracutaneous disease.

Children

- Unlike adult women, who commonly experience arthritis and arthralgias, only 8% to 10% of children develop joint symptoms.
- In children, large joints are affected more often than the small joints. The knees are the most commonly affected joints (82%), followed by ankles, wrists, elbows, neck, hands and feet, hips, shoulders, and sternoclavicular joints.
- The duration of joint symptoms is usually less than 4 months, but some have persistent arthritis for extended periods (2–13 months), fulfilling criteria for juvenile rheumatoid arthritis.

Pregnancy

- Approximately 50% to 60% of reproductive-age women are immune to parvovirus B19.
- Exposure to household members carries a 50% risk for seroconversion, whereas exposure from daycare or classroom work carries a 20% to 50% risk for seroconversion.
- When infection occurs during pregnancy, only 30% to 44% report signs (arthralgias and rash) of acute infection.

- The overall risk for fetal loss is 8% to 17% when infection occurs before 20 weeks and 2% to 6% after 20 weeks.
- An affected fetus can develop anemia, high-output cardiac failure, pleural effusions, polyhydramnios, and nonimmune hydrops fetalis.
- Overall, most parvovirus B19–infected mothers deliver healthy term infants.

Laboratory and Biopsy

- Detection of serum immunoglobulin M antibodies to parvovirus B19 using enzyme immunoassay is the most sensitive indicator of acute parvovirus B19 infection in immunocompetent hosts. These antibodies persist for up to 6 months.
- Polymerase chain reaction is the most sensitive method to detect parvovirus B19 and is the preferred method in immunocompromised hosts. These studies can be used to test fetal and maternal blood and amniotic fluid.
- Exposed pregnant women should have serologic or other diagnostic testing.
- Serial fetal ultrasounds should be performed on all pregnant women infected with parvovirus B19.

Differential Diagnosis

- Scarlet fever
- Enterovirus infection
- Rubella
- Rheumatoid arthritis (when there are joint symptoms)

Fig. 10.7 A, B, Erythema infectiosum. Net-like pattern of erythema.

Fig. 10.8 Facial erythema "slapped cheek." The red plaque covers the cheek and spares the nasolabial fold and the circumoral region.

Course and Prognosis

- Patients are not considered infectious after the rash develops.
- Most infections are self-limited without adverse sequelae.

Treatment

- Nonsteroidal anti-inflammatory drugs (NSAIDs) can control joint symptoms for most patients.
- Patients should be assured that this unusual eruption will fade and does not require treatment.
- If a fetus is affected, intrauterine evaluation and treatment are available at tertiary care centers.

Pediatric Considerations

- Children can return to child care and school when the rash appears.

Kawasaki Disease

Description

- Kawasaki disease, also known as *mucocutaneous lymph node syndrome,* is an acute multisystem vasculitis of unknown origin that occurs in infants and young children.
- The major causes of short-term and long-term morbidity are the cardiovascular manifestations.
- This condition occurs in both endemic and epidemic forms worldwide but is most common in Japan.
- Ages range from 7 weeks to 12 years (mean, 2.6 years); adult cases are rarely reported.
- Recurrences are rare.
- Diagnosis is often delayed in patients younger than 6 months and older than 5 years.

Centers for Disease Control and Prevention Diagnostic Criteria for Kawasaki Disease

- This diagnosis of the disease is based on having five of the following six clinical signs:
  - Fever of unknown origin for more than 5 days (95%)
  - Bilateral conjunctiva injection (87%–90%)
  - Changes of the lips and oral cavity (85%–95%)
  - Cervical lymphadenopathy greater than 1.5 cm (60%–70%)
  - Polymorphous exanthem with vesicles or crusts (85%–90%)
  - Changes of the peripheral extremities (90%–95%)
- If other diseases have been excluded and the patient has a coronary artery aneurysm, Kawasaki disease can be diagnosed with less than five of the six clinical signs.
- Infants younger than 6 months can have only prolonged fever and coronary artery aneurysms ("atypical Kawasaki disease"), making Kawasaki disease an important diagnostic consideration in all small infants with a fever of unknown origin.

Skin Findings

Conjunctival Injection

- Conjunctival injection occurs within 4 days of disease onset and subsides in 1 week.
- Uveitis occurs in 70% of cases.
- There is no purulent discharge or ulceration.

Changes in the Oral Mucous Membranes

- The lips and oral pharynx become red 3 to 5 days after the onset of the disease.
- The lips become dry, fissured, cracked, and crusted.
- Hypertrophic tongue papillae result in the "strawberry tongue" (80%), which is similar to that seen in scarlet fever.

Changes in the Extremities

- About 2 to 5 days after the onset of illness, the palms and soles become red, and the hands and feet become edematous (nonpitting). The tenderness can be severe enough to limit walking and use of the hands. The edema lasts for approximately 1 week.
- Desquamation of the hands and feet occurs 10 to 14 days after the onset of fever. The skin peels off in sheets, beginning around the fingernails and fingertips and progressing down to the palms and soles.
- Beau's lines may appear in the nails weeks later.

Rash

- A rash appears soon after the onset of fever.
- The rash is polymorphous because macules, papules, urticaria-like lesions, and erythema multiforme–like lesions have been described. Urticarial eruptions and diffuse, deep-red, maculopapular eruptions are the most common.
- Dermatitis in the diaper area is common and occurs in the first week. Red macules and papules become confluent. Desquamation occurs within 5 to 7 days.
- In children with inflammation of the diaper area, the skin peels at the margins of the rash and on the labia and scrotum.
- Perineal desquamation occurs 2 to 6 days before desquamation of the fingertips and toes.

Nonskin Findings

Fever

- Fever without chills or sweats lasts 5 to 30 days (mean, 8.5 days).

- The fever begins abruptly and spikes from 38.3° to 40° C and does not respond to antibiotics or antipyretics.

Cervical Lymphadenopathy

- Firm, nontender, nonsuppurative lymphadenopathy is often limited to a single cervical lymph node.

Cardiac Involvement

- Kawasaki disease is the major cause of acquired heart disease in children in the United States. If untreated, 20% to 25% of children develop coronary artery aneurysms.
- Early in the course of Kawasaki disease, more than 50% of patients develop myocarditis with tachycardia and gallop rhythms. These arrhythmias sometimes result in sudden death.
- In the subacute phase, aneurysm formation in medium-sized arteries, particularly the coronary arteries, is found in about one fourth of patients. These lesions may persist, scar with stenosis, or resolve angiographically. Aneurysms and thrombi form between 12 and 25 days after the onset and may result in congestive heart failure, pericardial effusions, arrhythmias, and death from myocardial ischemia or aneurysmal rupture.
- The abnormalities peak in the third week and often resolve thereafter.
- The prevalence of cardiac sequelae is high in male patients, in infants younger than 1 year of age, and children older than 5 years of age.
- Boys younger than age 1 year who have prolonged fever, elevated platelet counts, and high erythrocyte sedimentation rates are at greatest risk for coronary involvement.

Laboratory

- No diagnostic test exists.
- The acute phase is characterized by leukocytosis (20,000–30,000 cells/mm^3) with a left shift joint, thrombocytosis, and anemia.
- The erythrocyte sedimentation rate joint, C-reactive protein levels, and serum $alpha_1$-antitrypsin levels are elevated with the onset of fever and persist for up to 10 weeks.
- The platelet count begins to rise on day 10 of the illness, peaks at 600,000 cells/mL to 1.6 million cells/mL, and returns to normal by day 30.

Fig. 10.9 Kawasaki disease. The hands become red and swollen. The hands began to peel about 14 days after the onset of the erythema and swelling. (Courtesy of Nancy B. Esterly, MD.)

Course and Prognosis

- The worst prognosis occurs in children with so-called giant aneurysms, that is, those with a maximum diameter of more than 8 mm.
- Almost 10% of children do not improve clinically with treatment.

Treatment

- Intravenous immune globulin is given as a single infusion at a dose of 2 g/kg plus aspirin 30 to 80 mg/kg within the first 10 days from onset. The aspirin dose is decreased to 3 to 5 mg/kg as a single daily dose after the fever subsides. Treatment resolves clinical symptoms in 80% to 90% and reduces risk of coronary aneurysms to 2% to 4%.
- Approximately 10% of children are resistant to intravenous immune globulin. For these patients, methylprednisolone should be considered as an alternative to intravenous immune globulin.

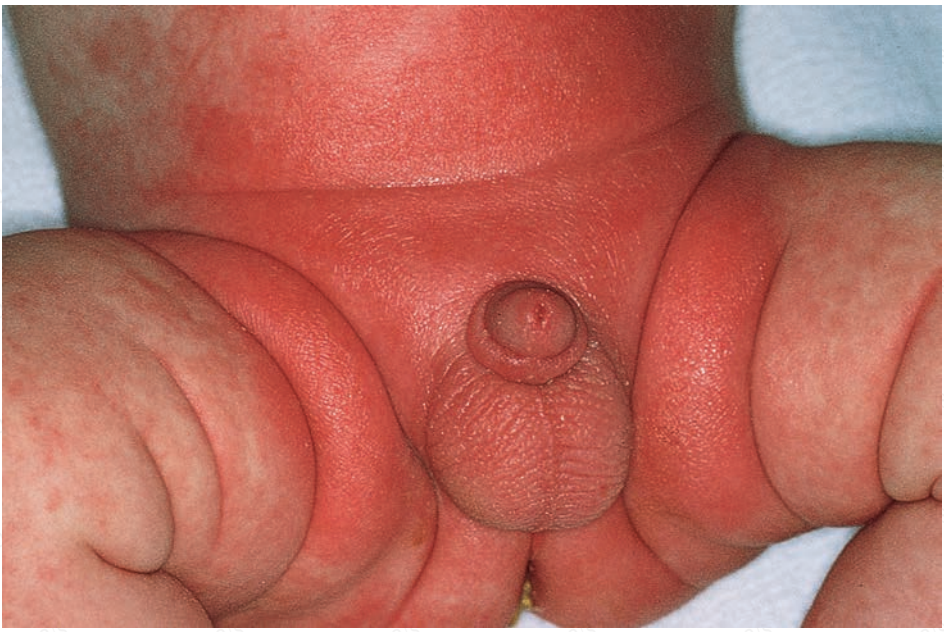

Fig. 10.10 Kawasaki disease. A diffuse, blanching, macular exanthem can appear and is often concentrated in the perianal area. This occurs 3 to 4 days after the onset of the illness. The rash becomes confluent and desquamates in 5 to 7 days. Peeling begins to occur at the margin of the rash. Desquamation of the fingertips and toes occurs 2 to 6 days later.

Fig. 10.11 Kawasaki disease. The hands peel approximately 2 weeks after the onset of fever. (Courtesy of Nancy B. Esterly, MD.)

Fig. 10.12 Kawasaki disease. Nonpurulent conjunctival injection and cherry-red lips with fissuring and crusting are early signs of the disease. (Courtesy of Anne W. Lucky, MD.)

Cutaneous Drug Reactions

Description

- Cutaneous drug reactions are common complications of drug therapy, and they can occur in many forms and can mimic many dermatoses.

History

- Cutaneous drug reactions are seen in 2% to 3% of hospitalized patients, most of whom are on multiple medications.
- The skin is the most commonly affected organ in adverse drug reactions.
- Fever may occur, and hours later a diffuse maculopapular rash, hives, generalized pruritus, or a combination of these develops.
- There is no correlation between the development of an adverse reaction and the patient's age, diagnosis, or survival.
- Drugs may be taken for weeks or years without ill effect, but when sensitization occurs, a reaction may occur within minutes to 24 to 48 hours.
- Chemically related drugs may cross-react in a patient sensitized to one agent.
- Two groups of mechanisms are mostly involved: immunologic (with all four types of hypersensitivity reactions described) and nonimmunologic (more common).

Morbilliform Eruptions

- The most frequent of all cutaneous drug reactions, maculopapular eruptions are often indistinguishable from viral exanthems.
- The onset occurs 7 to 10 days after starting the drug but may not occur until after the drug is stopped. The rash lasts 1 to 2 weeks and fades, in some cases even if the drug is continued.
- Maculopapular eruption, red macules, and papules become confluent in a symmetric, generalized distribution that often spares the face. Itching is common. The mucous membranes, palms, and soles may be involved.
- Symptoms are treated with antihistamines and cooling lotions (e.g., Sarna lotion).

Urticarial Drug Reactions

- Aspirin, penicillin, and blood products are the most frequent causes of urticarial drug eruptions, but almost any drug can cause hives.
- Anaphylactic immunoglobulin E–dependent reactions occur within minutes (immediate reactions) to hours (accelerated reactions) of drug administration.
- In circulating immune complex disease (serum sickness), urticaria occurs 4 to 21 days after drug ingestion; hives typically fade in less than 24 hours, only to recur in another area. After the drug is stopped, this problem resolves over several weeks.
- Nonimmunologic histamine reactions can occur in minutes; the allergenic drug or agent (e.g., morphine, codeine, polymyxin B, lobster, strawberries) may exert a direct action on the mast cell.
- Symptoms are treated with antihistamines and cooling lotions (e.g., Sarna lotion); topical steroids do not help.
- Hospitalization, observation, intubation, and epinephrine (adrenaline) all may be needed for severe reactions.

Internal–External Reactions

- The patient first develops a contact dermatitis with a topical agent and subsequently develops either a focal flare or a generalized eruption when exposed orally

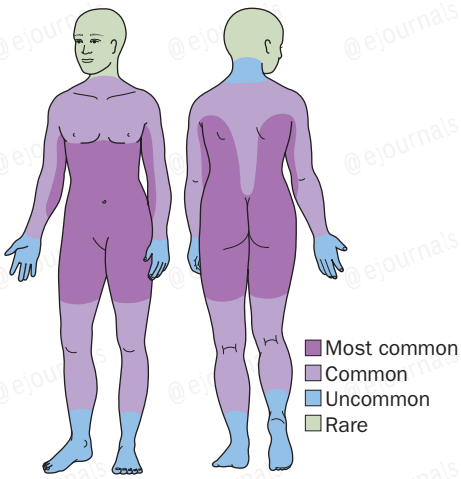

Fig. 10.13 Cutaneous drug reactions distribution diagram.

to the same or chemically related medication.
- Continued use of the medication can intensify the reaction and lead to generalization of the eruption.
- Eczematous internal–external reaction usually presents as areas of redness, particularly in the axillae or groin.
- Topical or oral steroids control these eruptions.

Erythema Multiforme and Toxic Epidermal Necrolysis Reactions

- The lesions of erythema multiforme look like targets. Bullae develop in severe forms of the disease.
- These reactions may be limited to the skin or mucous membranes but can be generalized.
- Severe forms are often caused by medications. Mycoplasmal pneumonia, herpes simplex infections, and medications cause less severe forms.
- Toxic epidermal necrolysis can be severe and fatal. The cause of death is loss of large areas of skin, resulting in fluid loss and sepsis.
- Severe reactions are best managed in burn units or intensive care units.
- The use of oral steroids is controversial.

Exfoliative Erythroderma

- There is generalized redness and desquamation.
- The reaction is potentially life-threatening.

Fig. 10.14 Cutaneous drug reactions. The glans penis is a common location for a fixed drug reaction.

Fig. 10.15 Cutaneous drug reactions. Pigmentation from minocycline contains melanin or iron and can be found on the lower extremities, within scars and on sun-exposed areas.

Fixed Drug Eruptions

- Single or multiple, round, sharply demarcated, dusky-red plaques appear soon after drug exposure and reappear in exactly the same site each time the drug is taken.
- The lesions are generally preceded or accompanied by itching and burning, which may be the only manifestations of reactivation in an old patch.
- The area often blisters and then erodes; desquamation or crusting (after bullous lesions) follows, and brown pigmentation forms with healing.
- Lesions can occur on any part of the skin or mucous membrane, but the glans penis is the most common site. Tetracycline, co-trimoxazole, and NSAIDs frequently cause fixed lesions or fixed drug eruptions on the glans penis.
- The length of time from re-exposure to a drug and the onset of symptoms is 30 minutes to 8 hours.
- After each exacerbation, some patients experience a refractory period (weeks to several months), during which time the offending drug does not activate the lesions.
- A careful history is important because patients often do not relate their complaints to the use of a drug.
- "Provoking" or challenging the appearance of the lesion with the suspected drug confirms the diagnosis, prevents recurrences, and allays the anxiety of the patient regarding a venereal origin of disease.

Box 10.1 Drug Reactions and the Drugs That Cause Them

Maculopapular (Exanthematous) Eruptions

- Ampicillin
- Antiretrovirals
- Barbiturates
- Diflunisal (Dolobid)
- Gentamicin
- Gold salts
- Human epidermal receptor inhibitors
- Isoniazid
- Meclofenamate (Meclomen)
- Phenothiazines
- Phenylbutazone
- Phenytoin (5% of children; dose dependent)
- Quinidine
- Sulfonamides
- Thiazides
- Tyrosine kinase inhibitors
- Thiouracil
- Trimethoprim–sulfamethoxazole (in patients with AIDS)

Anaphylactic Reactions

- Aspirin
- Penicillin
- Radiographic dye
- Sera (animal derived)

Serum Sickness

- Aspirin
- Penicillin
- Streptomycin
- Sulfonamides
- Thiouracils

Acneiform (Pustular) Eruptions

- Bromides
- Hormones
  - Adrenocorticotropic hormone
  - Androgens
  - Corticosteroids
  - Oral contraceptives
- Iodides
- Isoniazid
- Lithium
- Phenobarbital (aggravates acne)
- Epidermal growth factor receptor antibodies (cetuximab)
- Phenytoin

Alopecia

- Allopurinol
- Anticoagulants
- Antithyroid drugs
- Chemotherapeutic agents
  - Alkylating agents
  - Antimetabolites
  - Cytotoxic agents
- Colchicine
- Hypocholesteremic drugs
- Indomethacin
- Levodopa
- Oral contraceptives
- Propranolol
- Quinacrine
- Retinoids
- Thallium
- Vitamin A

Erythema Nodosum

- Iodides
- Oral contraceptives
- Sulfonamides

Exfoliative Erythroderma

- Allopurinol
- Arsenicals
- Barbiturates
- Captopril
- Cefoxitin
- Chloroquine
- Cimetidine
- Gold salts
- Hydantoins
- Isoniazid
- Lithium
- Mercurial diuretics
- Para-aminosalicylic acid
- Phenylbutazone
- Sulfonamides
- Sulfonylureas

Fixed Drug Eruptions

- Aspirin
- Barbiturates
- Methaqualone
- Phenazones
- Phenolphthalein
- Phenylbutazone
- Sulfonamides
- Tetracyclines
- Trimethoprim–sulfamethoxazole
- Nonsteroidal anti-inflammatory drugs (NSAIDs)
- (Many others reported)

Lichen Planus–Like Eruptions

- Antimalarials
- Arsenicals
- Beta-blockers
- Captopril
- Furosemide
- Gold salts
- Methyldopa
- Penicillamine
- Quinidine

Box 10.1 Drug Reactions and the Drugs That Cause Them—cont'd

- Sulfonylureas
- Thiazides

Erythema Multiforme–Like Eruptions

- Allopurinol
- Barbiturates
- Carbamazepine
- Hydantoins
- Minoxidil
- Nitrofurantoin
- NSAIDs
- Penicillin
- Phenolphthalein
- Phenothiazines
- Rifampin
- Sulfonamides
- Sulfonylureas
- Sulindac

Lupus-Like Eruptions

Common

- Hydralazine
- Procainamide

Probable

- Acebutolol
- Carbamazepine
- Ethosuximide
- Lithium carbonate
- Penicillamine
- Phenytoin
- Propylthiouracil
- Sulfasalazine

Uncommon

- Chlorpromazine
- Hydrochlorothiazide
- Isoniazid
- Methyldopa
- Quinidine

Photosensitivity

- Amiodarone
- Carbamazepine
- Chlorpropamide
- Furosemide
- Griseofulvin
- Lomefloxacin
- Methotrexate (sunburn reactivation)
- Nalidixic acid
- Naproxen
- Phenothiazines
- Piroxicam (Feldene)
- Psoralens
- Quinine
- Sulfonamides
- Tetracyclines
- Demeclocycline
- Doxycycline (less frequently with tetracycline and minocycline)
- Thiazides
- Tolbutamide

Skin Pigmentation Disorders

- Adrenocorticotropic hormone (brown as in Addison's disease)
- Amiodarone (slate-gray)
- Anticancer drugs
  - Bleomycin (30%; brown, patchy, linear)
  - Busulfan (diffuse as in Addison's disease)
  - Cyclophosphamide (nails)
  - Doxorubicin (nails)
- Antimalarials (blue-gray or yellow)
- Arsenic (diffuse, brown, macular)
- Chlorpromazine (slate-gray in sun-exposed areas)
- Clofazimine (red)
- Heavy metals
  - Bismuth
  - Gold
  - Mercury
  - Silver
- Methysergide maleate (red)
- Minocycline (patchy or diffuse blue-black)
- Oral contraceptives (chloasma-brown)
- Psoralens
- Rifampin (very high dose; red man syndrome)

Pityriasis Rosea–Like Eruptions

- Arsenicals
- Barbiturates
- Bismuth compounds
- Captopril
- Clonidine
- Gold compounds
- Methoxypromazine
- Metronidazole
- Pyribenzamine

Toxic Epidermal Necrolysis

- Allopurinol
- Phenylbutazone
- Phenytoin
- Sulfonamides
- Sulindac

Small Vessel Cutaneous Vasculitis

- Allopurinol
- Diphenylhydantoin
- Hydralazine
- Penicillin

Continued

Box 10.1 Drug Reactions and the Drugs That Cause Them—cont'd

- Piroxicam (Feldene) (Henoch–Schönlein purpura)
- Propylthiouracil
- Quinidine
- Sulfonamides
- Thiazides

Vesicles and Blisters

- Barbiturates (pressure areas; comatose patients)
- Bromides
- Captopril (pemphigus-like)
- Cephalosporins (pemphigus-like)
- Clonidine (cicatricial pemphigoid–like)
- Furosemide (phototoxic)
- Iodides
- Nalidixic acid (phototoxic)
- Naproxen (like porphyria cutanea tarda)
- Penicillamine (pemphigus foliaceus–like)
- Phenazones
- Piroxicam (Feldene)
- Sulfonamides

Ocular Pemphigoid

- Demecarium bromide
- Echothiophate iodide
- Epinephrine
- Idoxuridine
- Pilocarpine
- Timolol

Chemotherapy-Induced Acral Erythema

- Cyclophosphamide
- Cytosine arabinoside
- Doxorubicin
- Fluorouracil
- Hydroxyurea
- Mercaptopurine
- Methotrexate
- Mitotane
- Sorafenib
- Sunitinib

Drug-Induced Hyperpigmentation

- Drug-induced hyperpigmentation is caused by many different drugs, including antiarrhythmics (amiodarone), antimalarials, antibiotics (minocycline), antivirals (zidovudine), antiseizure agents (hydantoin), chemotherapy agents, heavy metals, hormones, and antipsychotics (chlorpromazine). The discoloration often fades with time (months to years).
- Amiodarone causes a dusky-red coloration that with time becomes blue-gray or ashen. This is usually in photodistributed areas.
- Minocycline (Minocin) causes a blue-gray or slate-gray discoloration, often in acne lesions, but also on the gingiva or any area of the skin.
- Zidovudine causes brown longitudinal pigmentation on the nails and a similar brown color on the lips and oral mucosa.
- Antimalarial agents typically cause a brown discoloration on the shins or elsewhere.
- Hydantoin may cause melasma-like brown pigmentation on the face.
- Bleomycin causes a dramatic reaction, including a flagellate, streaking hyperpigmentation on the trunk and extremities.
- Melasma, a typical brown pigmentation on the cheeks and central face, is associated with oral contraceptive use. The use of a broad-spectrum ultraviolet B and ultraviolet A sunscreen is advisable in many of these cases.

Lichenoid Drug Reactions

- The clinical and histologic patterns mimic those of lichen planus.
- The latent period between the beginning of administration of a drug and the eruption is 3 weeks to 3 years.
- There are multiple flat-topped, itchy violaceous papules; oral lesions may be present.
- Lesions heal with brown pigmentation.
- Gold and antimalarial agents are most often associated with drug-induced lichen planus.
- The lesions are chronic and persist for weeks or months after the offending drug is stopped.

Photosensitivity Drug Eruptions

- Both systemic and topical medications can induce photosensitivity.
- There are two main types: phototoxicity and photoallergy.
- Phototoxic reactions are related to drug concentration and can occur in anyone. They can occur on first administration and subside when the drug is stopped. The eruption is confined to sun-exposed areas.

There is erythema within 24 hours of light exposure.
- Photoallergic reactions are less common and are not related to concentration. There is a delay of 48 hours after exposure before the eruption appears. The eruption can spread to non–sun-exposed regions.

Onycholysis
- Onycholysis is separation of the nail plate from the nail bed.
- It may occur from drug photosensitivity and has occurred after the administration of tetracyclines, psoralens, and fluoroquinolones.

Small Vessel Necrotizing Vasculitis (Palpable Purpura)
- Small vessel necrotizing vasculitis may be precipitated by drugs.
- Lesions are most often concentrated on the lower legs.
- Vessels of the kidneys, joints, and brain may be involved.

Chemotherapy-Induced Acral Erythema
- Tingling on the palms and soles is followed in a few days by painful, symmetric, well-defined swelling and erythema.
- The hands are more severely affected than the feet.
- Areas of pallor develop, blister, desquamate, and re-epithelialize.
- Chemotherapy-induced acral erythema occurs most commonly after the administration of cytosine arabinoside, fluorouracil, and doxorubicin.
- The reaction is dose dependent, and a direct toxic effect of the drug is likely.

Fig. 10.16 Maculopapular eruption. Maculopapular drug eruptions are often indistinguishable from viral exanthems. Ampicillin may cause diffuse macules and papules, but several other drugs also cause this pattern.

Fig. 10.17 Erythema multiforme. The classic ring-like eruption on the palms.

Fig. 10.18 Urticarial eruption. Drugs are a common cause of hives.

Fig. 10.19 Acute generalized exanthematous pustulosis. Antibiotics, especially beta-lactams and macrolides, are the main culprits.

Fig. 10.20 Acute generalized exanthematous pustulosis. Numerous pustules appeared 5 days after penicillin was started. The medication was stopped, and the pustules cleared spontaneously in 2 weeks.

- The time of onset is 24 hours to 10 months, and the severity varies.
- Cytosine arabinoside has a predilection to progress to blisters.
- Treatment is supportive and includes elevation and cold wet dressings.
- Systemic steroids have been used with variable success.
- Cooling the hands and feet during treatment to decrease blood flow may attenuate the reaction.
- Modification of the dosage schedule may also help.

Acute Generalized Exanthematous Pustulosis

- Acute generalized exanthematous pustulosis is characterized by multiple tiny superficial pustules over most of the body.
- The most common drugs involved are the antibacterial agents (mostly penicillin).
- There is a short interval between drug ingestion and the eruption (mean, 5 days), and resolution occurs in less than 15 days.
- Fever, leukocytosis, and an ill-appearing patient are common.
- Desquamation occurs with no scarring.
- Simple lubrication of the skin, along with removal of the offending drug, is all that is needed.

Fig. 10.21 Photosensitivity drug eruption. Erythema and papules occurred on exposed areas in this patient who had been taking a thiazide antihypertensive medication.

Fig. 10.22 Photosensitivity drug eruption. Red papules in a symmetric photodistribution in a patient taking amiodarone.

Fig. 10.23 Fixed drug eruption. Single or multiple, round, sharply demarcated, dusky-red plaques appear soon after drug exposure and reappear in exactly the same site each time the drug is taken.

Fig. 10.24 Viral exanthem. Classic viral exanthems may be clinically indistinguishable from a macularpapular drug eruption.

Toxic Shock Syndrome

Description

- Toxic shock syndrome is an acute toxin-mediated multisystem disease resulting in high fever, diffuse erythroderma, mucous membrane hyperemia, and profound hypotension.

History

- In the past, most patients with toxic shock syndrome were women of reproductive age who were vaginally infected or colonized with a toxin-producing strain of *Staphylococcus aureus* (phage group 1; TSST-1, enterotoxin B, A, C1). Symptoms occur within 4 days of menses, and the risk is higher with use of high-absorbency tampons.
- Toxin-producing strains of *Streptococcus pyogenes* (M protein types 1, 3, 12, 28; toxins SPE-A or SPE-B) can produce toxic shock syndrome (streptococcal toxic shock syndrome). In this syndrome, the infectious focus is often the skin or soft tissue, and many patients are bacteremic.
- Non–menstruation-related toxic shock syndrome accounts for 20% to 30% of toxic shock syndrome cases. On average, symptoms occur 7 days after the precipitating event. Patients with bacterial tracheitis (especially after an infection with influenza B virus) and burns appear to be at higher risk for non–menstruation-related toxic shock syndrome.
- Toxic shock syndrome has been described in association with surgical and nonsurgical wound infections, abortion, childbirth, use of nasal packing, and contraceptive sponges.
- In all forms of toxic shock syndrome, susceptible hosts appear to have low to absent levels of toxin-specific antibodies and local factors that favor toxin production.

Skin Findings

- In toxic shock syndrome, a scarlatiniform rash develops on the torso and spreads to the extremities within 1 to 3 days of disease onset. Early in the course of the disease, there may be edema of the hands and feet (50%), petechiae (27%), conjunctival injection (85%), oropharyngeal hyperemia (90%), and genital hyperemia (100%). One or 2 weeks after disease onset, many patients develop a generalized itchy morbilliform eruption involving the palms and soles, but the face is spared. Desquamation of the palms, soles, fingertips, and toes occurs 10 to 21 days after the onset.
- In streptococcal toxic shock syndrome, 80% of patients have cutaneous signs of soft tissue infection, and 70% have deep soft tissue infections, such as necrotizing fasciitis, that require immediate surgical débridement.

Nonskin Findings

- In toxic shock syndrome, patients acutely develop high fever, abdominal pain, vomiting, headache, and myalgias, leading to profound hypotension and multiorgan failure.
- In toxic shock syndrome children develop respiratory distress more commonly than adults.

Laboratory and Biopsy

- Hematologic and serum chemistry abnormalities reflect multiorgan damage.
- Skin microscopic findings are not specific for toxic shock syndrome.
- A skin biopsy should be done to distinguish toxic shock syndrome from toxic epidermal necrolysis and drug hypersensitivity reaction.

Differential Diagnosis

- Drug eruptions
- Kawasaki disease
- Infantile polyarteritis nodosa
- Scarlet fever
- Staphylococcal scalded skin syndrome
- Toxic epidermal necrolysis
- Viral exanthema

Course and Prognosis

- With prompt antibiotic and supportive therapy, the mortality rate is low: overall, 3.7%; in men, 12.2%; and in women, 2.6%.

Treatment

- The goal of therapy in toxic shock syndrome is to minimize organ damage through

supportive management of shock and medical and surgical treatment of infection.

- In toxic shock syndrome, beta-lactamase–resistant antimicrobial antibiotics (oxacillin, nafcillin, cefoxitin, vancomycin, clindamycin) are administered intravenously. In 3 to 5 days most patients are able to tolerate oral antibiotics, which are continued for a total of 10 to 14 days.
- Intravenous immune globulin has been helpful in some patients because of neutralizing antibodies.

Box 10.2 Toxic Shock Syndrome Case Definition

Major Criteria (All Four Must Be Met)

- **Fever:** temperature >38.9°C (102°F)
- **Rash:** diffuse or palmar erythroderma progressing to subsequent peripheral desquamation (hands and feet)
- **Mucous membrane:** nonpurulent conjunctival hyperemia, or oropharyngeal hyperemia, or vaginal hyperemia or discharge
- **Hypotension:** systolic blood pressure less than 90 mm Hg for an adult (>16 years of age) or less than 5th percentile for age for a child; or orthostatic hypotension as shown by a drop in diastolic blood pressure greater than 15 mm Hg from recumbent to sitting; or history of orthostatic dizziness

Multisystem Involvement (Three or More Must Be Present)

- **Gastrointestinal:** history of vomiting or diarrhea at onset of illness
- **Muscular:** creatinine phosphokinase >2 × upper limit of normal for laboratory values 4 to 20 days after onset
- **Central nervous system:** disorientation or alteration in consciousness without focal signs at a time when patient is not in shock or hyperpyrexic
- **Renal:** blood urea nitrogen or serum creatinine clearance levels >2 × upper limit of normal; and abnormal findings on urinalysis (>5 white blood cells per high-power field; >1 red blood cell per high-power field; protein >1+); or oliguria defined as urine output <1 mL/kg/hour for 24 hours.
- **Hepatic:** total serum bilirubin level of >1.5 × upper limit of normal; or serum glutamate pyruvate transaminase levels of >2 × upper limit of normal
- **Hematologic:** thrombocytopenia (platelets less than 100,000/mm^3)
- **Cardiopulmonary:** adult respiratory distress syndrome; or pulmonary edema; or new-onset second-degree or third-degree heart block; or electrocardiogram criteria for myocarditis decreased voltage and ST–T wave changes; or heart failure shown by new onset of gallop rhythm, or by increase in size of cardiac silhouette from one chest roentgenogram to another during the course of the illness, or diagnosed by cardiologist
- **Metabolic:** serum calcium level less than 7 mg/dL with serum phosphate level less than 2.5 mg/dL, and total serum protein level less than 5 mg/dL

Evidence for Absence of Other Causes

- **When obtained:** negative blood, throat, urine, or cerebrospinal fluid cultures
- **When obtained:** absence of serologic evidence of leptospirosis, rickettsial disease, or rubeola
- **Evidence for absence of Kawasaki disease:** no unilateral lymphadenopathy or fever lasting more than 10 days

From Chesney RW, Chesney PJ, Davis JP, Segar WE. Clinical manifestations of toxic shock syndrome. *JAMA* 1981;246(7):741–748.

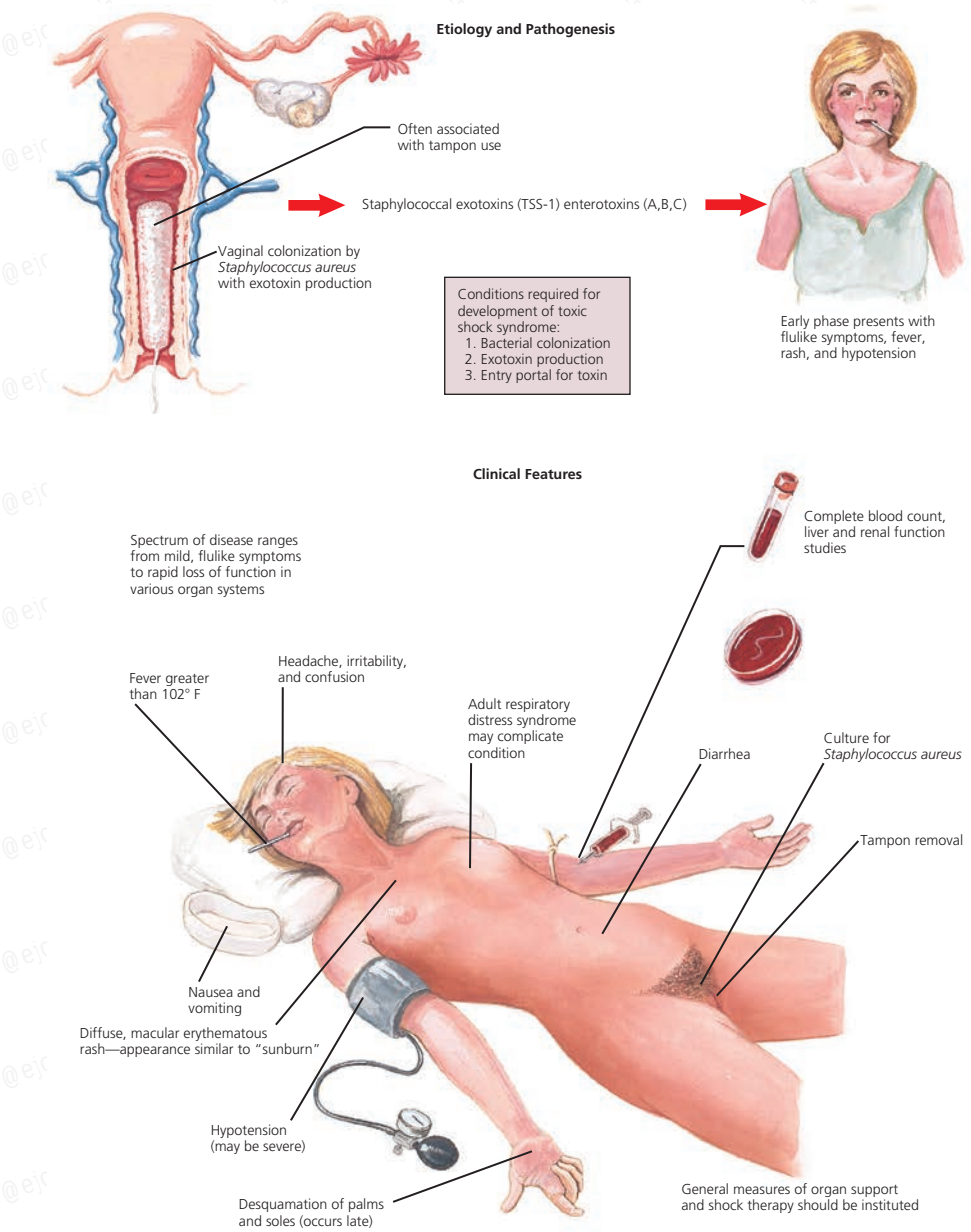

Fig. 10.25 Toxic shock syndrome. (Netter illustration from www.netterimages.com. ©)

Fig. 10.26 Fixed drug eruption. This child developed a fixed drug eruption after taking trimethoprim–sulfam ethoxazole. The history of antibiotic use helps distinguish fixed drug eruption from granuloma annulare.

Fig. 10.27 Amiodarone rash. Amiodarone may cause slate-gray pigmentation.

Fig. 10.28 Lichenoid drug eruption. Skin biopsy showed a lichenoid drug eruption. Lichenoid drug eruptions may last months after stopping the causative medication.

Fig. 10.29 Lichenoid drug eruption. Lichenoid drug eruptions are a deep-pink to purple with a small amount of scale.

Fig. 10.30 Penicillin eruption. Diffuse morbilliform eruption due to penicillin.

11 Hypersensitivity Syndromes and Vasculitis

James G. H. Dinulos

Erythema Multiforme

Description

- Erythema multiforme is a relatively common, acute—often recurrent—inflammatory disease characterized by target-shaped skin lesions.

History

- Commonly, erythema multiforme is associated with herpes simplex, *Mycoplasma pneumoniae,* and upper respiratory tract infections, although erythema multiforme may be associated with many conditions (Table 11.1).
- Rarely, erythema multiforme is associated with contact allergens, drugs, connective tissue diseases, physical agents, x-ray therapy, pregnancy, and internal malignancies.
- The cause of erythema multiforme is unknown in at least half of the patients.
- A minority of patients with reactivation of herpes simplex develop recurrent erythema multiforme.
- Erythema multiforme is thought to be produced by a cytotoxic immune response directed against keratinocytes expressing foreign viral or drug antigens.

Skin Findings

- As its name suggests, erythema multiforme shows numerous lesion morphologies: target lesions, erythematous macules and papules, urticarial-like lesions, vesicles, and bullae.
- Patients should only be diagnosed clinically with erythema multiforme if target lesions are seen.
- Target lesions begin as dusky-red, round macules and papules that may burn and itch.
- These early lesions appear suddenly in a symmetric pattern on the palms, soles, backs of the hands and feet, and the extensor aspect of the forearms and legs. The diagnosis of erythema multiforme may not be suspected until the nonspecific early lesions evolve into target lesions during a period of 24 to 48 hours.
- The classic "iris" or target lesion results from centrifugal spread of the red maculopapule to a circumference of 1 to 3 cm. The center of the iris can appear dark red, purpuric, or vesicular and is due to acute epidermal injury. This central area is surrounded by a pale area of edematous skin, which is in turn surrounded by a sharp discrete ring of erythema.
- Lesions appear in crops, resolving in 1 to 2 weeks without scarring.
- Postinflammatory pigment changes are common (hypopigmentation and/or hyperpigmentation).
- Bullae and erosions may be present in the oral cavity.
- The urticarial plaques seen in erythema multiforme are distinguished from hives in that they are fixed and do not resolve in 24 hours.
- Erythema multiforme lesions may occur in areas of trauma (Koebner's phenomenon).

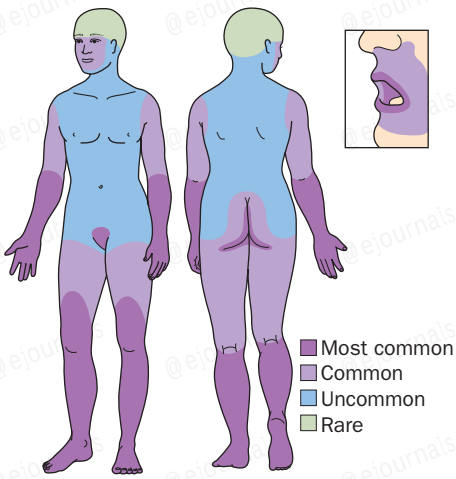

Fig. 11.1 Erythema multiforme distribution diagram.

Table 11.1 Etiologic Factors for Developing Erythema Multiforme

Infections in approximately 90% of cases	Viral in descending order of incidence	Herpes viruses: herpes simplex virus types 1 and 2, Epstein–Barr virus, cytomegalovirus, varicella-zoster virus Adenoviruses Enteroviruses: coxsackievirus B5, echoviruses
	Bacterial in descending order of incidence	*Mycoplasma pneumonia* *Corynebacterium diphtheria* Hemolytic streptococci *Legionella pneumophila* *Salmonella* species *Mycobacterium leprae* *Pneumococcus* species
Drugs (<10% of cases)	Highly suspected in descending order of incidence	Sulfonamides (trimethoprim, sulfamethoxazole) Nonsteroidal anti-inflammatory drugs Penicillins Anticonvulsants (barbiturates, carbamazepine) Hydantoids Valproic acid Allopurinol Antifungal (terbinafine) Oxicam* (piroxicam, tenoxicam)
	Others	Imidazole Chlormezanone Systemic corticosteroids Cephalosporins Quinolones Tetracycline
Immune condition	Immune disease	Graft-versus-host disease Inflammatory bowel disease Polyarteritis nodosa Sarcoidosis Systemic lupus erythematosus
	Immunization	Bacille Calmette-Guérin, Hepatitis B and smallpox immunization
Others	Food additives	Benzoates Nitrobenzene
	Chemicals	Perfume Terpenes

*Members of a class of nonsteroidal anti-inflammatory drugs that bind closely to plasma proteins.
From Samin F, Auluck A, Zed C, Williams PM. Erythema multiforme: a review of epidemiology, pathogenesis, clinical features, and treatment. *Dent Clin North Am* 2013;57(4):583–596.

Nonskin Findings

- Erythema multiforme may be preceded by cough, malaise, and fever and may be associated with pneumonia.

Laboratory and Biopsy

- Laboratory testing is not necessary. Vesicles or erosions suggestive of herpes simplex confirmed by viral culture or direct immunofluorescence.
- Skin biopsy shows an interface reaction with necrotic keratinocytes and can be helpful when the diagnosis is uncertain.

Course and Prognosis

- Usually, erythema multiforme resolves within 1 month.

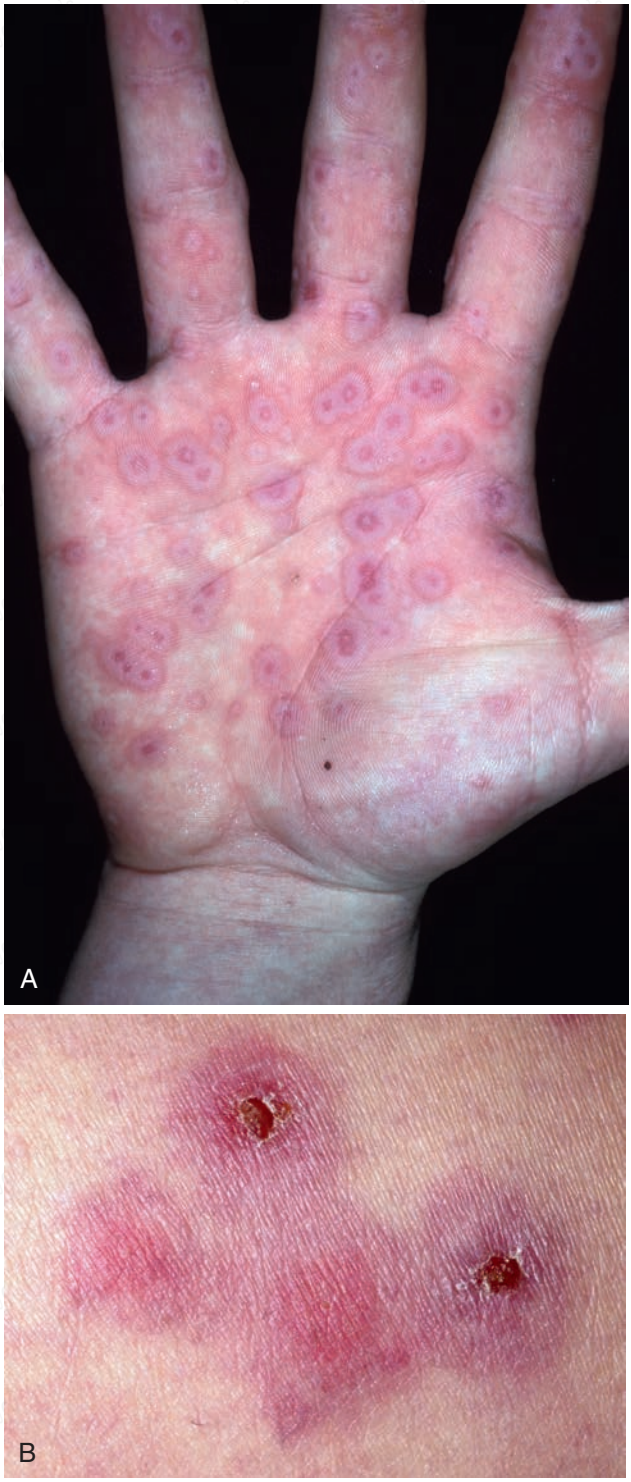

Fig. 11.2 Erythema multiforme. **A, B,** A dusky red macule or urticarial papule expands to about 2 cm over 24 to 48 hours. A papule, vesicle, or bulla develops in the center, then flattens and may clear. The periphery becomes cyanotic to form the classic target lesion.

Fig. 11.3 Erythema multiforme. The palms, back of the hands, and extensor forearms are a common place to find the initial target lesions. Erythema multiforme can be precipitated by a herpes simplex virus infection.

- Patients who develop erythema multiforme associated with reactivated herpes simplex may require suppressive therapy to prevent recurrences.

Treatment

- Most patients with erythema multiforme do not require treatment.
- Ruptured blisters and eroded skin can be treated with local measures, such as topical antibiotics.
- Widespread erythema multiforme responds rapidly to 1 to 3 weeks of systemic corticosteroids. Prednisone 40 to 80 mg/day should be administered until lesions resolve, and then tapered as appropriate.
- Recurrent herpes-associated erythema multiforme can be prevented by administering oral acyclovir (200 mg two or three times a day or 400 mg twice a day), valacyclovir (Valtrex), 500 mg/day, or famciclovir (Famvir) 125 mg twice daily as continuous suppressive therapy.

Stevens–Johnson Syndrome and Toxic Epidermal Necrolysis

Description

- Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN) are two conditions characterized by epidermal necrosis with varying degrees of body surface area (BSA) (SJS < 10% BSA, SJS/TEN overlap 10%–30% BSA, and TEN >30% BSA).

History

- SJS is three times more common than TEN.
- The mortality rate of SJS is 10% and more than 30% for TEN.
- Drug reactions account for 80% to 95% of cases of TEN. The most frequently associated drugs are co-trimoxazole and other sulfonamides, lamotrigine, carbamazepine, phenytoin, phenobarbital, sulfasalazine, aminopenicillins, cephalosporins, quinolones, oxicam nonsteroidal anti-inflammatory drugs, allopurinol, and nevirapine.
- On average, TEN occurs 2 weeks after initiation of the drug.
- Those infected with HIV have a 1000-fold increased risk for TEN, which in part may be related to antiretroviral use.
- Certain autoimmune conditions such as systemic lupus erythematosus appear to be at greater risk for drug-induced TEN.
- TEN can be precipitated by a recent immunization (diphtheria–pertussis–tetanus, measles, poliomyelitis, influenza), viral infection (cytomegalovirus, Epstein–Barr virus, herpes simplex, varicella-zoster, hepatitis A, dengue), mycoplasmal infection, streptococcal infection, syphilis, histoplasmosis, coccidioidomycosis, and tuberculosis.
- Acute graft-versus-host disease and contrast medium can be associated with TEN.
- TEN is caused by CD8 T-cell–mediated cell death in susceptible hosts.

Skin Findings

- Most patients develop diffusely red "sunburn-like" tender skin with scattered target lesions and bullae. Bullae quickly coalesce, resulting in widespread skin sloughing.
- Full-thickness epidermal necrosis and detachment (necrolysis) leave a tender glistening raw surface.
- Gentle lateral pressure easily produces epidermal detachment.
- Mucous membranes develop exquisitely painful erosions.
- Cutaneous sequelae of TEN include dyspigmentation, eruptive melanocytic nevi, onychodystrophy, and hair thinning.

Nonskin Findings

- Findings include ocular (sicca syndrome, symblepharon, corneal scarring, blindness), pulmonary (chronic bronchitis and respiratory tract obstruction), oral (reduced salivary flow, periodontal disease), genitourinary system (dyspareunia, vaginal adhesions, balanitis and genitourinary strictures), and gastrointestinal system (esophageal strictures).

Laboratory and Biopsy

- A skin biopsy can be helpful to distinguish between TEN and staphylococcal scalded skin syndrome. Sloughed skin can be "jelly-rolled" onto a round wooden applicator and sent for frozen section. This quick and simple test will show a superficial epidermal split in staphylococcal scalded skin syndrome and a full-thickness necrotic epidermis in TEN.
- A skin biopsy sent for direct immunofluorescence can distinguish between TEN and autoimmune blistering conditions, such as paraneoplastic pemphigus.

Differential Diagnosis

- Staphylococcal scalded skin syndrome
- Graft-versus-host disease
- Staphylococcal toxic shock syndrome
- Kawasaki disease
- Acute-onset paraneoplastic pemphigus

Course and Prognosis

- SJS/TEN can be preceded by fever, malaise, cough, and abdominal pain.

- Predictors of poor outcome include old age, widespread blistering, immunodeficiency, neutropenia, impaired renal function, and multiple medications.
- Overall, the mortality rate for TEN is 30% to 50%.
- The mortality rate for acute graft-versus-host disease–associated TEN is nearly 100%.

Treatment

- Treatment regimens focus on controlling pain, identifying and treating sources of infection, withdrawing suspected offending medications, maintaining fluid and nutritional requirements, and providing meticulous local wound care. If possible, severely affected patients should be managed in a burn unit.

Pediatric Considerations

- Treatment principles are the same in children as they are in adults.
- Overall, children have a lower mortality rate than adults.

Fig. 11.5 Stevens–Johnson syndrome. Skin lesions are flat, atypical targets, or purpuric maculae, that are widespread or distributed on the trunk. Lesions in this extensive case have become eroded and infected.

Fig. 11.4 Stevens–Johnson syndrome. Severe bullous form. Bullae are present on the conjunctiva and in the mouth.

Fig. 11.6 Stevens–Johnson syndrome. Exudative conjunctivitis seen in this adolescent boy must be treated with ophthalmic ointment to prevent adhesions.

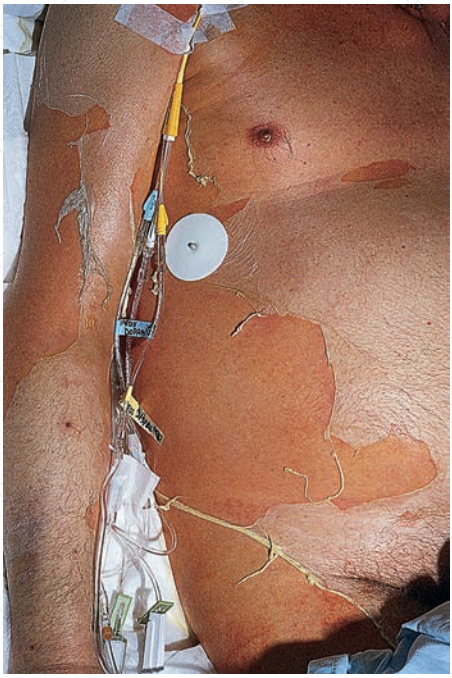

Fig. 11.7 Shedding of full-thickness epidermis in toxic epidermal necrolysis.

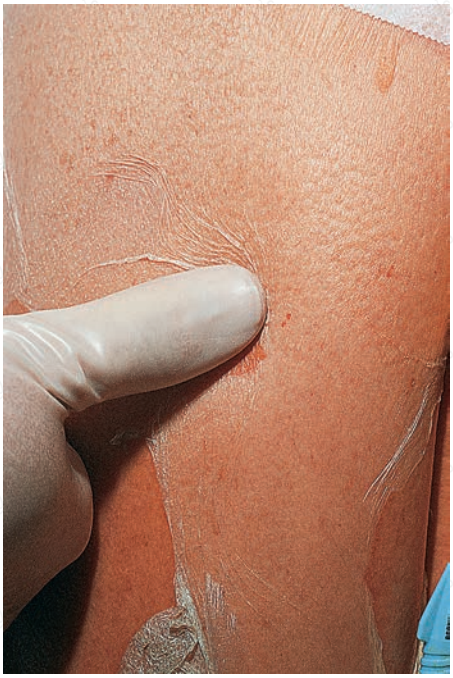

Fig. 11.8 Wrinkling with slight pressure in toxic epidermal necrolysis (Nikolsky's sign).

Erythema Nodosum

Description

- Erythema nodosum is a panniculitis characterized by tender pink nodules on the extensor surface of the lower legs.

History

- In adults, erythema nodosum is five or six times more common in women, and the peak age of onset is 20 to 30 years of age. In children, boys and girls are affected equally.
- Erythema nodosum is thought to be due to a hypersensitivity reaction to a variety of antigenic stimuli.
- Many bacteria, viruses, fungi, parasites, drugs, malignancies, and connective tissue diseases have been associated with erythema nodosum (Box 11.1). In the United States streptococcal infections and sarcoidosis are commonly associated with erythema nodosum.
- Half of cases are idiopathic.

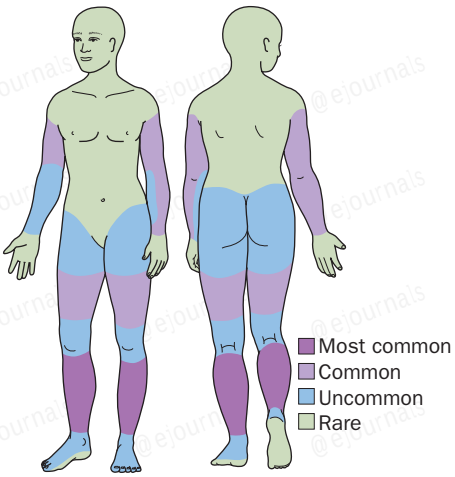

Fig. 11.9 Erythema nodosum distribution diagram.

Skin Findings

- Erythema nodosum is characterized by pink to dusky-red firm nodules with indistinct edges, occurring symmetrically on the pretibial surfaces. Erythema nodosum can occur on the head, neck, torso, arms, and thighs.
- Erythema nodosum fades over a period of 1 to 2 weeks, similar to a bruise, and does not leave residual scars.
- Ankle edema and leg pain are common.

Box 11.1 Erythema Nodosum: Associated Conditions and Medications

Infections

Bacterial infections
- Streptococcal
- Tuberculosis
- *Yersinia*
- *Mycoplasma*
- Psittacosis
- Brucellosis
- *Campylobacter*
- *Shigella*
- *Salmonella*
- Leprosy
- Leptospirosis
- Tularemia

Viral infections
- Epstein–Barr virus
- Hepatitis B
- Orf
- Herpes simplex virus
- *Bartonella*

Fungal infections
- Coccidioidomycosis
- Blastomycosis
- *Histoplasmosis*
- Sporotrichosis
- Dermatophytosis

Parasitic infections
- Ascariasis
- Amebiasis
- Giardiasis

Drugs
- Sulfonamides
- Oral contraceptives
- Bromides
- Iodides
- Minocycline
- Gold
- Penicillin
- Salicylates

Malignancies
- Lymphoma
- Leukemia
- Renal cell carcinoma
- Postirradiation therapy

Inflammatory Conditions
- Sarcoidosis
- Ulcerative colitis
- Crohn's disease
- Behçet's disease
- Sweet's syndrome

Fig. 11.10 Erythema nodosum. Red, node-like swelling is seen in the characteristic distribution.

Fig. 11.11 Erythema nodosum. Lesions begin as red, node-like swellings over the shins; as a rule, both legs are affected. The border is poorly defined, with size varying from 2 to 6 cm.

Nonskin Findings

- Erythema nodosum may be associated with fever, malaise, diarrhea, headache, conjunctivitis, and cough.

Laboratory and Biopsy

- Laboratory evaluation should be guided by history and physical examination. Initial tests should include a throat culture or rapid test for *Streptococcus,* a complete blood count, and a chest radiograph.
- A deep skin biopsy to include fat can be helpful in patients with atypical lesions.
- Chest radiograph may show bilateral hilar adenopathy. This finding can be present in erythema nodosum due to sarcoidosis as well as other diseases.

Differential Diagnosis

- Cellulitis
- Infected insect bites
- Minor trauma
- Other forms of panniculitis
- Henoch–Schönlein purpura
- Superficial and deep thrombophlebitis
- Vasculitis

Course and Prognosis

- New crops of lesions usually develop for 3 to 6 weeks, although, rarely erythema nodosum can persist for months to years.

Treatment

- Associated diseases and infections should be identified and treated. Precipitating medications should be discontinued.
- Usually, symptoms can be relieved with rest, compressive bandages, and nonsteroidal anti-inflammatory drugs (indomethacin, naproxen).
- Supersaturated potassium iodide and systemic corticosteroids have been helpful for chronic recurrent erythema nodosum. Erythema nodosum improves within 48 hours and resolves within 2 weeks with 300 to 900 mg daily of potassium iodide.

Cutaneous Small Vessel Vasculitis (Hypersensitivity Vasculitis)

Description

- Cutaneous small vessel vasculitis describes a group of disorders characterized by inflammation of small blood vessels in the skin, primarily postcapillary venules. The principal skin lesion is palpable purpura.

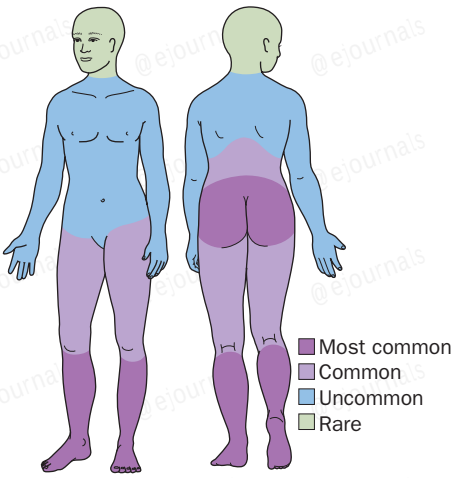

Fig. 11.12 Cutaneous small vessel vasculitis distribution diagram.

History

- Cutaneous small vessel vasculitis is precipitated by many infectious agents, drugs, chemicals, and food allergens (Box 11.2) and is associated with many chronic connective tissue diseases and malignancies (Box 11.3).
- In 60% of patients, no precipitating agent or coexistent disease is identified.
- Cutaneous small vessel vasculitis is caused by deposition of immunoglobulin G (IgG) or IgM immune complexes in small postcapillary venules.

Skin Findings

- Early lesions show minimal blood vessel damage and are seen as asymptomatic purpuric macules.
- With time and more vessel damage, lesions coalesce and become edematous and palpable, ranging in size from less than a millimeter to several centimeters. Purpuric papules, nodules, pustules, vesicles, bullae, and ulcerations can occur.
- Lesions may occur on any dependent area or an area under local pressure (e.g., the back and arms of supine patients). They are uncommon on the face, palms, and soles.

Box 11.2 Precipitating Agents for Cutaneous Small Vessel Vasculitis

Infections

Bacteria
- Beta-hemolytic group A *Streptococcus*
- *Staphylococcus aureus*

Viruses
- Hepatitis A, B, and C viruses
- Herpes simplex virus
- Influenza virus

Fungi
- *Candida albicans*

Protozoa
- *Plasmodium malaria*

Helminths
- *Schistosoma haematobium*
- *Schistosoma mansoni*
- *Onchocerca volvulus*

Drugs
- Insulin
- Penicillin
- Hydantoins
- Streptomycin
- Aminosalicylic acid
- Sulfonamides
- Thiazides
- Phenothiazines
- Vitamins
- Phenylbutazone
- Quinine
- Streptokinase
- Tamoxifen
- Anti-influenza vaccines
- Oral contraceptives
- Serum

Chemicals
- Insecticides
- Petrolatum products

Foodstuff Allergens
- Milk proteins
- Gluten

Adapted from Lotti T, Ghersetich I, Comacchi C, Jorizzo JL. Cutaneous small-vessel vasculitis. *J Am Acad Dermatol* 1998;39:667–687.

Box 11.3 Conditions Associated With Cutaneous Small Vessel Vasculitis

Chronic Diseases
- Systemic lupus erythematosus
- Sjögren's syndrome
- Rheumatoid arthritis
- Behçet's disease

Hyperglobulinemic States
- Cryoglobulinemia
- Bowel bypass syndrome
- Ulcerative colitis
- Cystic fibrosis
- Primary biliary cirrhosis
- HIV seropositivity and AIDS

Malignant Neoplasms
- Lymphoproliferative disorders
- Hodgkin's disease
- Mycosis fungoides
- Lymphosarcoma
- Adult T-cell leukemia
- Multiple myeloma

Solid Tumors
- Lung cancer
- Colon carcinoma
- Renal cancer
- Prostate cancer
- Head and neck cancer
- Breast cancer

Adapted from Lotti T, Ghersetich I, Comacchi C, Jorizzo JL. Cutaneous small-vessel vasculitis. *J Am Acad Dermatol* 1998;39:667–687.

- Lesions can be itchy and painful and occur in crops.
- Frequently, patients develop ankle and lower leg edema.

Nonskin Findings

- Commonly, arthralgias, myalgias, fever, and malaise accompany each crop of lesions.
- Immune complexes deposit in the kidneys, gastrointestinal tract, lungs, heart, nervous system, joints, and eyes, causing multiorgan damage.

Laboratory and Biopsy

- Laboratory testing should be directed by history and physical examination findings. Baseline laboratory testing should examine other organ systems for the presence of vasculitis and coexistent disease. Initial screening should include a chest radiograph, a complete blood count, liver enzymes, total protein, blood urea nitrogen, creatinine, electrolytes, serum calcium, uric acid, erythrocyte sedimentation rate, antinuclear antibody, and urinalysis.
- The erythrocyte sedimentation rate is always elevated during active vasculitis.
- A skin biopsy will show leukocytoclastic vasculitis.

Differential Diagnosis

- Thrombocytopenic purpura
- Drug eruptions
- Disseminated intravascular coagulation
- Purpura fulminans
- Septic vasculitis
- Septic emboli
- Bacteremia

Course and Prognosis

- Cutaneous small vessel vasculitis usually subsides within 1 month. However, some patients develop chronic, intermittent crops of lesions for years.

Treatment

- Removal of precipitating agents and appropriate treatment of coexistent disease usually result in resolution of cutaneous small vessel vasculitis.
- Local measures using topical steroids and antibiotics help some patients.
- Antihistamines and nonsteroidal anti-inflammatory drugs are useful to control fever, myalgias, and arthralgias.
- Systemic corticosteroids (prednisone 60–80 mg/day) are helpful for managing systemic manifestations and skin ulceration. Rebound can be prevented with a slow taper over 3 to 6 weeks.
- Immunosuppressive agents (cyclophosphamide, methotrexate, azathioprine, and cyclosporine) have been used when systemic corticosteroids fail.

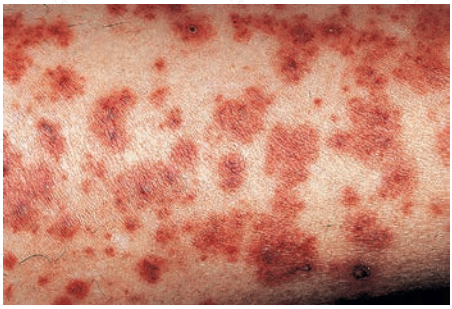

Fig. 11.13 Cutaneous small vessel vasculitis. Purpura is the first sign of hypersensitivity vasculitis. Lesions vary in size from pinpoint to several centimeters. They then become papular, nodular, vesicular, bullous, pustular, or ulcerated as superficial infarctions occur. This gives the lesions substance that can be palpated, thus the term *palpable purpura*.

Fig. 11.14 Cutaneous small vessel vasculitis. Purpura are most often found on the lower extremities in small vessel hypersensitivity vasculitis.

Fig. 11.15 Cutaneous small vessel vasculitis. Purpura vary from pinpoint to several centimeters. This is an early case with minimal swelling.

Fig. 11.16 Cutaneous small vessel vasculitis. A few to numerous discrete, purpuric lesions are most commonly seen on the lower extremities but may occur on any dependent area, including the back if the patient is bedridden, or the arms.

Fig. 11.17 Cutaneous small vessel vasculitis. Lesions are most often found on the legs and about the ankles. They appear in crops and are all in the same stage. Edema usually occurs soon after the appearance of the palpable purpura. Lesions are mildly pruritic or painful. They resolve in 3 or 4 weeks and leave hyperpigmentation and atrophic scars.

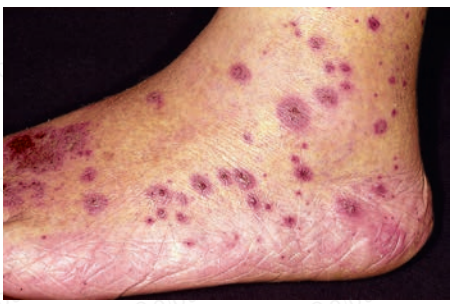

Fig. 11.20 Vasculitis. Hypersensitivity vasculitis produces palpable purpura and small blisters.

Fig. 11.18 Vasculitis. Severe hypersensitivity vasculitis may result in bulla and erosions.

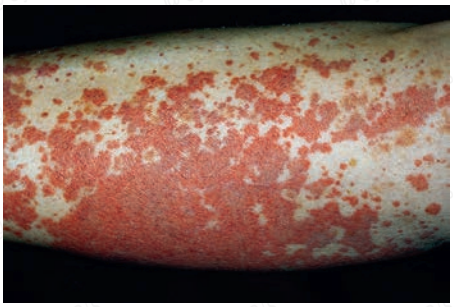

Fig. 11.19 Vasculitis. Purpuric papules may coalesce into large plaques in hypersensitivity vasculitis.

Fig. 11.21 Vasculitis. Hypersensitivity vasculitis may produce palpable purpura of varying sizes on the lower extremity.

Immunoglobulin a Vasculitis (Henoch–Schönlein Purpura)

Description

- IgA vasculitis is a leukocytoclastic small vessel vasculitis due to deposition of IgA immune complexes in postcapillary venules. It occurs primarily in children.
- IgA vasculitis is characterized by palpable purpura, joint pain, abdominal pain, and glomerulonephritis.

History

- IgA vasculitis and Kawasaki disease are the two most common forms of childhood vasculitis. Ninety percent of IgA vasculitis occurs in children younger than 10 years. Boys between 4 and 8 years of age are at highest risk.
- In children, the peak incidence is during the fall and winter months, commonly following an acute respiratory illness by 1 to 2 weeks.
- In adults, the peak incidence is during the winter and summer months.

Skin Findings

- Skin lesions begin as symmetric pink to red macules that quickly evolve into purpuric papules.
- They are pinhead sized to 2 cm and characteristically occur on the buttocks and lower extremities.
- Like other forms of cutaneous small vessel vasculitis, IgA vasculitis lesions occur in crops and fade within 2 weeks.
- Edema of the hands and feet can be prominent.
- Children younger than 3 years can develop striking edema around the eyes, scalp, and ears.

Nonskin Findings

- Up to 2 weeks before the onset of purpura, 40% of children develop low-grade fever, headache, arthralgias, and abdominal pain.
- Arthralgias (80%), abdominal pain (70%), and renal changes (45%) are the most common extracutaneous sites of infection.
- Rarely, patients develop other system disorders, including seizures and neurologic deficits, pulmonary hemorrhage, myocarditis, hepatomegaly, parotitis, adrenal necrosis, and hydrops of the gallbladder.
- Fewer than 5% of children are at risk from massive gastrointestinal bleeding and ilioileal intussusception (especially older children).
- Boys can develop scrotal edema. Scrotal pain can occur before the purpura, making it difficult to distinguish from testicular torsion.

Laboratory and Biopsy

- Diagnosis is based on the typical clinical features.
- In atypical cases, a skin biopsy will show leukocytoclastic vasculitis. A skin biopsy should be sent for direct immunofluorescence, looking for IgA immune complex deposition.
- Helpful initial laboratory tests include complete blood count, coagulation studies, blood urea nitrogen, creatinine, liver enzymes, bilirubin, amylase, lipase, and urinalysis.
- Patients with severe abdominal pain should be evaluated for intussusception with an abdominal ultrasound. Further diagnostic evaluation should be done in consultation with a specialist in gastroenterology or surgery.
- Patients with high blood pressure or laboratory signs of nephritis should be seen in consultation with a nephrologist.

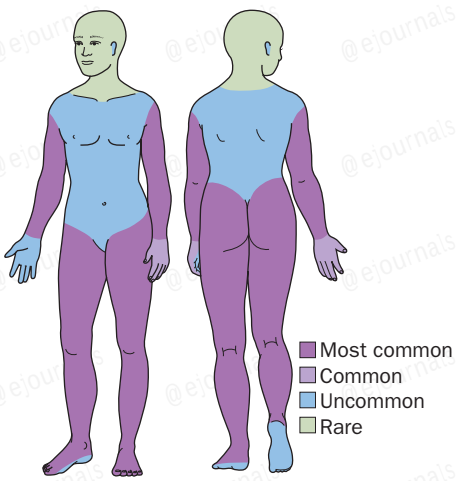

Fig. 11.22 Henoch–Schönlein purpura distribution diagram.

Differential Diagnosis

- Bacterial sepsis
- Hemolytic uremic syndrome
- Poststreptococcal glomerulonephritis
- Rocky Mountain spotted fever or other rickettsial disease
- Other forms of cutaneous small vessel vasculitis

Course and Prognosis

- Most children have self-limited disease, lasting less than 1 month.
- Long-term prognosis may be determined by the degree of renal involvement.
- Adults undergo relapse in 20% of cases and are at higher risk for renal disease than children.

Treatment

- Nonsteroidal anti-inflammatory drugs can be helpful to manage arthralgias.
- Systemic corticosteroids and immunosuppressive agents may be indicated in patients with severe renal and gastrointestinal complications.

Pediatric Considerations

- Quick referrals should be made to the appropriate specialists in children with severe abdominal pain and evidence of nephritis.
- Children should be followed closely for renal involvement, checking blood pressure and urinalysis for 3 months after the purpura resolves.

Fig. 11.23 Henoch–Schönlein purpura. Scattered palpable purpura on the lower extremities is the hallmark of this leukocytoclastic vasculitis.

Fig. 11.24 Henoch–Schönlein purpura may result in lower extremity swelling and palpable purpura.

Fig. 11.25 Henoch–Schönlein purpura is a systemic vasculitis characterized by palpable purpura, colicky abdominal pain, gastrointestinal hemorrhage, arthralgias, and renal involvement. Palpable purpura are most often seen on the lower extremities and buttocks, but they may appear on the upper body.

Schamberg's Disease (Schamberg's Purpura)

Description

- Schamberg's disease, a form of progressive pigmented purpura, is a lymphocytic capillaritis characterized by petechiae and brown purpuric patches, occurring most commonly on the lower extremities.

History

- Schamberg's disease slowly evolves on the distal lower extremities and progresses proximally.
- In adults, men are more commonly affected. In children, girls are more commonly affected.
- Schamberg's disease is a lymphocytic capillaritis, suggesting a cell-mediated hypersensitivity.

Skin Findings

- Patients develop multiple distinct orange-brown, pinhead-sized "cayenne pepper" macules with numerous petechiae. Lesions occur symmetrically on the lower extremities and sometimes on the upper body.
- New petechiae are bright red, becoming violaceous with age and leaving brown dots of hemosiderin pigmentation.
- Schamberg's disease can be asymmetric, especially when seen in adolescence.
- There may be a slight amount of erythema, scale, and itching.

Nonskin Findings

- Schamberg's disease is an isolated skin disorder.

Laboratory and Biopsy

- Laboratory testing is not necessary.
- A skin biopsy can be done to exclude leukocytoclastic vasculitis.
- Skin microscopy shows a perivascular mononuclear cell infiltrate with extravasated red blood cells.

Differential Diagnosis

- Cutaneous T-cell lymphoma
- Nummular eczema
- Scurvy
- Senile purpura
- Contact dermatitis
- Drug-induced purpura
- Stasis dermatitis
- Factitial dermatitis

Course and Prognosis

- Schamberg's disease is a chronic condition without internal disease. Most patients improve with time.

Treatment

- Pigmentation can be covered with cosmetic creams, such as Dermablend.
- There are no consistently effective therapies, although the following have been administered:
  - Group V topical steroids
  - Pentoxifylline (Trental) 300 mg per day for 8 weeks
  - Rutoside (oral bioflavonoid) 50 mg twice daily and ascorbic acid 500 mg twice daily for 8 weeks

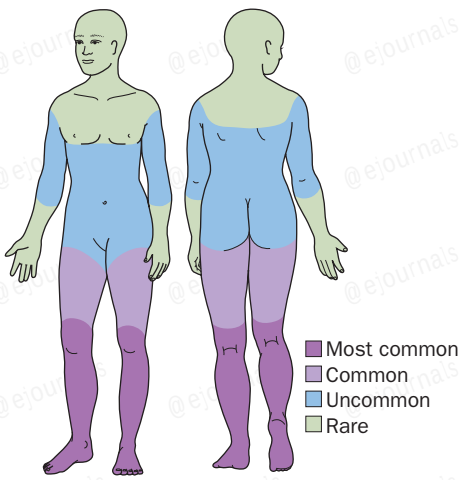

Fig. 11.26 Schamberg's disease distribution diagram.

Fig. 11.27 Schamberg's disease. Asymptomatic, irregular patches of varying shapes and sizes occur most often on the lower extremities. The most characteristic feature is the orange-brown, pin-sized "cayenne pepper" spots.

Fig. 11.28 Schamberg's disease. The lesions begin as asymptomatic, localized areas of cutaneous hemorrhage that acquire substance and become palpable as blood leaks out of damaged vessels.

Fig. 11.29 Schamberg's disease. These changes are more subtle and resemble the hyperpigmentation seen with stasis dermatitis.

Fig. 11.30 Schamberg's disease. The distribution is haphazard. The "cayenne pepper" spots are not as prominent as seen in the previous figures.

Sweet's Syndrome

Description

- Sweet's syndrome is an acute inflammatory eruption characterized by multiple pink to red tender plaques, associated with fever, malaise, and leukocytosis.

History

- Sweet's syndrome occurs in adults of all ages (mean age, 56 years) but is uncommon in children.
- The disease onset is preceded by an upper respiratory infection in many patients.
- Sweet's syndrome is paraneoplastic (hematologic malignancy, solid tumors) in 15% to 20% of patients and may precede the malignancy by up to 6 years.
- Paraneoplastic Sweet's syndrome can affect mucous membranes, tends to be recurrent, and occurs more commonly in males.
- Other associated conditions include streptococcal infection, inflammatory bowel disease, autoimmune disorders (Hashimoto's thyroiditis, Sjögren's syndrome), myelodysplastic syndrome, and acute myelomonocytic leukemia.
- Sweet's syndrome has been associated with pregnancy.
- Sweet's syndrome may be caused by medications, including granulocyte colony-stimulating factor, isotretinoin, trimethoprim–sulfamethoxazole, bortezomib, azathorpine, ketoconazole, nitrofurantoin, and ciprofloxacin.

Skin Findings

- Sweet's syndrome lesions erupt acutely and can be painful. They are plum colored and "juicy" (pseudovesicular) in appearance.
- They can occur on any skin surface but tend to occur on the head, neck, legs, arms, dorsal hands, and fingers.

Nonskin Findings

- Systemic symptoms include body temperature higher than 38°C (50%), malaise, arthralgias, or arthritis (62%), eye involvement (conjunctivitis, episcleritis, iridocyclitis) (33%), and oral aphthae (13%).
- Rarely, neutrophilic infiltrates occur within the upper respiratory tract, lungs, liver, kidneys, and brain.

Laboratory and Biopsy

- Complete blood count, comprehensive metabolic panel, erythrocyte sedimentation rate, and urinalysis should be performed.
- Appropriate testing for malignancy-associated Sweet's syndrome should be done based on history and physical examination findings.
- Common laboratory abnormalities include white blood cell count of 8000 cells/mL with greater than 70% polymorphonucleocytes, increased erythrocyte sedimentation rate, and elevated alkaline phosphatase (40%).
- Skin biopsy shows an abundance of neutrophils in the dermis with marked subepidermal edema without vasculitis.

Differential Diagnosis

- Erythema multiforme
- Erythema nodosum
- Adverse drug reaction
- Urticaria

Course and Prognosis

- Sweet's syndrome can be self-limited in some patients.

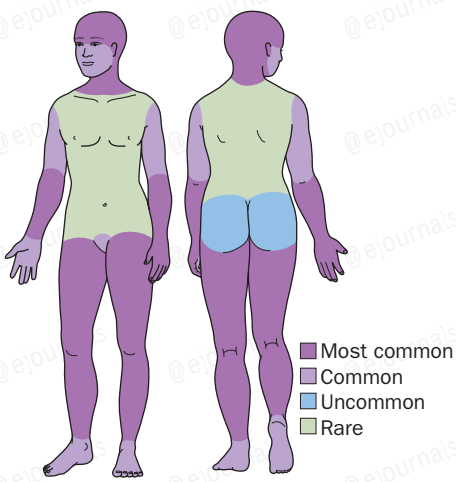

Fig. 11.31 Sweet's syndrome distribution diagram.

- Sweet's syndrome responds quickly to systemic corticosteroids. Typically, laboratory values correct within 72 hours and skin lesions clear within 3 to 9 days.
- Fifteen percent of patients intermittently relapse for several years.

Treatment

- Systemic corticosteroids (prednisone 0.5–1.5 mg/kg/day) produce rapid improvement and can be tapered over 2 to 6 weeks.
- Minocycline 100 mg twice a day, or doxycycline 100 mg twice a day, may be effective.
- Oral potassium iodide 15 mg/kg/day inhibits neutrophil chemotaxis and equals systemic corticosteroids in effectiveness.
- Other therapies include colchicine, dapsone, clofazimine, nonsteroidal anti-inflammatory drugs, and cyclosporine.
- Underlying malignancy and associated medications must be identified and removed when present.

Fig. 11.32 Sweet's syndrome. Acute, tender, erythematous plaques, nodes, pseudovesicles, and occasionally, blisters with an annular or arciform pattern occur on the extremities. The trunk is sometimes involved in extensive cases.

Fig. 11.33 Sweet's syndrome. Lesions are tender erythematous papules and plaques that can also be pseudovesicular or pustular. Pustules occur on or adjacent to the lesions. Lesions tend to be multiple, but isolated lesions are seen. Plaques usually measure a few centimeters, but larger lesions up to 20 cm in diameter occur.

Fig. 11.34 Atypical Sweet's syndrome (also known as *neutrophilic dermatosis* of the dorsal hands) is a recently described disorder. Severely painful, purulent blue to purple nodules and plaques frequently accompanied by ulceration occur on the dorsal hands. Oral corticosteroids are effective, antibiotics are not.

Fig. 11.35 Pyoderma gangrenosum. Pyoderma gangrenosum appears similar to Sweet's syndrome and can be differentiated with a skin biopsy.

Panniculitis

Description

- Panniculitis refers to a group of disorders that cause inflammation of the subcutaneous fat.

History

- Typically, panniculitis occurs in association with an underlying systemic disorder or in association with a cutaneous disease. Rarely, panniculitis occurs as a primary idiopathic process.

Skin Findings

- Panniculitis manifests as discrete pink to deep red, tender nodules and firm plaques.
- Some forms of panniculitis cause extensive skin necrosis and breakdown (calciphylaxis).

Nonskin Findings

- Nonskin findings vary with the type of panniculitis.

Laboratory and Biopsy

- Laboratory evaluation should be guided by the history and physical examination.
- In most patients, a skin biopsy is an essential part of the diagnostic evaluation for panniculitis. An early lesion should be excised deep enough to include full-thickness skin and abundant fat. A deep excisional biopsy provides an adequate specimen.

Differential Diagnosis

- Selected forms of panniculitis include the following:
  - Erythema nodosum
  - Alpha$_1$-antitrypsin deficiency panniculitis
  - Cold-induced panniculitis
  - Neonatal subcutaneous fat necrosis
  - Pancreatic panniculitis
  - Lupus panniculitis
  - Sarcoidosis
  - Calcifying panniculitis of renal failure (calciphylaxis)
  - Fungal and bacterial panniculitis
  - Polyarteritis nodosa
  - Lipodermatosclerosis
  - Leukemia and lymphoma

Course and Prognosis

- The course and prognosis depends on the type of panniculitis.

Treatment

- Panniculitis associated with an underlying systemic condition improves with treatment of the condition. Other forms of panniculitis (erythema nodosum and cold-induced panniculitis) are self-limited and do not require anything more than symptomatic treatment (see erythema nodosum) (Box 11.4).

Box 11.4 Histopathologic Classification of the Panniculitides

Mostly Septal Panniculitides

- Cutaneous polyarteritis nodosa
- Erythema nodosum
- Leukocytoclastic vasculitis
- Necrobiosis lipoidica
- Necrobiotic xanthogranuloma
- Rheumatoid nodule
- Scleroderma
- Subcutaneous granulosa annulare
- Superficial thrombophlebitis

Mostly Lobular Panniculitides

- $Alpha_1$-antitrypsin deficiency
- Calciphylaxis
- Cold panniculitis
- Crohn's disease
- Crystal-storing histiocytosis
- Cytophagic histiocytic panniculitis
- Erythema induratum of Bazin
- Erythema nodosum leprosum
- Factitial panniculitis
- Gout panniculitis
- Infective panniculitis
- Lipoatrophy
- Lucio's phenomenon
- Lupus panniculitis (lupus erythematosus profundus)
- Neutrophilic lobular (pustular) panniculitis associated with rheumatoid arthritis
- Oxalosis
- Pancreatic panniculitis
- Panniculitis in dermatomyositis
- Postirradiation pseudosclerodermatous panniculitis
- Poststeroid panniculitis
- Sclerema neonatorum
- Sclerosing panniculitis
- Subcutaneous fat necrosis of the newborn
- Subcutaneous sarcoidosis
- Traumatic panniculitis

Adapted from Requena L, Yus ES. Panniculitis. Part I. Mostly septal panniculitis. *J Am Acad Dermatol* 2001;45:163–183.

Infestations and Bites 12

M. Shane Chapman

Scabies

Description

- Scabies is a parasitic infestation of the skin caused by the mite *Sarcoptes scabiei* var. *hominis.*
- It is characterized by an intensely pruritic eruption and may be the etiology of "the 7-year itch."

History

- Patients with scabies complain of a rash with unremitting itching and an inability to stop scratching, even while being examined.
- It is uncommon for scabies to present in just one member of a family.
- Usually, several other members of the family, usually with close contact, especially bed partners, will also have symptoms.
- Nodular lesions take the longest to heal or completely resolve.
- Crusted scabies (thousands of mites) may be the source of epidemic scabies and is seen in institutionalized or immunocompromised patients.
- Persistent itching after adequate treatment is due to a prolonged allergic response to mite feces and body parts.

Skin Findings

- A linear or curved burrow is the classical lesion of scabies; it is a linear, curved, or S-shaped slightly elevated vesicle or papule up to 1 to 2 mm wide.
- Burrows and other scabies lesions are most likely to be found in the intertriginous areas, finger webs, wrists, sides of the hands and feet, lateral fingers and toes, and genitalia, including the glans penis, buttocks, and scrotum.
- The palms, soles, and scalp may be more commonly affected in infants than adults.
- Scabies may also present with scattered inflamed pustules, linear vesicles, papules, and even larger nodules.
- Individual lesions may be excoriated, hemorrhagic, and crusted.
- The scabies rash and associated pruritus usually appear 2 to 6 weeks after exposure.
- Eczema and impetigo may appear as a secondary consequence.
- A unique, advanced clinical variant is crusted (Norwegian) scabies. Patients—usually those with dementia, Down syndrome, or immunosuppression—experience thick crusting and eczematous dermatitis, especially on the hands and feet. These lesions contain numerous mites.

Laboratory and Testing

- Mites, eggs, or feces can be identified in a scabies preparation.
- A scabies preparation involves applying mineral oil to a burrow, vesicle, or papule to preserve the mite feces. The burrow is scraped with a #15 blade and rubbed on a glass slide, a coverslip is placed on top, and the slide is viewed microscopically.
- Potassium hydroxide and heat (performed for identification of tinea) will make mites easier to identify but will destroy mite feces.
- Mites are not always easily identified, and sometimes body parts, feces, or eggs are more easily visualized for confirmation.

Differential Diagnosis

- Eczema
- Xerosis
- Drug rash
- Insect bites
- Impetigo
- Folliculitis
- Lymphomatoid papulosis

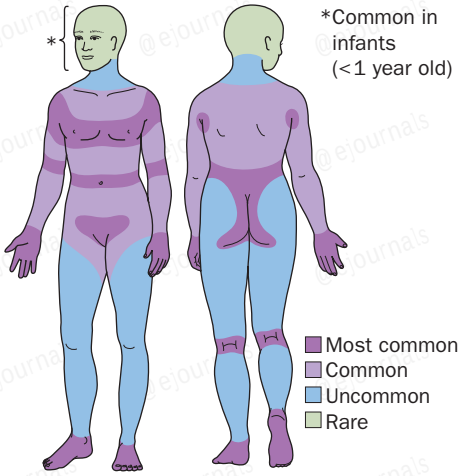

Fig. 12.1 Scabies distribution diagram.

Fig. 12.2 Scabies: vesicles and burrows. Burrows are most likely to be found in the finger webs, wrists, sides of the hands and feet, penis, buttocks, scrotum, and palms and soles of infants.

Fig. 12.3 Scabies: burrow. The linear, curved, or S-shaped burrows are approximately as wide as #2 suture material and are 2 to 15 mm long. A drop of ink can accentuate them.

Fig. 12.4 Scabies: vesicles and pustules. Scattered vesicles and pustules, with superficial scale, on the plantar surfaces of infants are a common presentation of scabies.

Fig. 12.5 Scabies: secondary lesions result from infection or are caused by scratching. Scaling, erythema, and all stages of eczematous inflammation occur as a response to excoriation or to irritation caused by overzealous attempts at self-medication.

Treatment

- Permethrin or lindane is applied to the entire skin surface from the neck down, including under the fingernails and toenails and in the umbilicus.
- The patient should bathe after about 12 hours. This regimen should be repeated in 1 week. Lindane should be used with caution in infants because of reports of neurotoxicity. Lindane is not available in the United Kingdom.
- Malathion lotion 0.5 is effective and is used in a similar manner as permethrin.
- A standard program in developing countries consists of a bath with monosulfiram soap, followed by application of benzyl benzoate lotion to the entire body below the neck. This is washed off in 24 hours and then repeated daily for 3 to 5 consecutive days.

It may cause irritant dermatitis, especially in the genital area and on the face. There is no evidence for adverse effects on pregnancy outcome. It is not available in the United States.

- The head and neck are uncommonly affected, but if lesions are present there and need treatment, care should be taken to avoid the eyes and mouth.
- All clothes and bedding must be washed in hot water or put in a hot dryer at the time of antiscabetic application.
- There is no need for fumigation or extermination treatments in the house.
- A single dose of oral ivermectin (Stromectol 6-mg scored tablet) (200 mcg/kg) is also safe and effective for most patients. Repeating the dose in 1 to 2 weeks is a common practice and may provide a higher cure rate. Combination of ivermectin with topical treatment may also provide a higher cure rate.
- Ivermectin should be used with caution in the treatment of scabies in elderly patients.
- Topical steroids may be used to control pruritus and inflammation after complete treatment with a scabicide.
- Persistent nodular lesions can be treated with intralesional steroids.
- Posttreatment pruritus can occur for weeks or months, even though the mites have been cleared.

Pearls

- Scabies should be considered for any generalized itchy eruption unresponsive to prednisone or any pruritic rash that gets worse with steroid treatment.
- Even adequately treated scabies may continue to itch for days to weeks after treatment, and it does not need to be retreated in all cases. Rescraping should be performed if incomplete treatment or reinfection is suspected.

Fig. 12.6 Scabies. *Sarcoptes scabiei* in a potassium hydroxide wet mount (×40).

Fig. 12.7 Elderly man with scabies. Infestation became much worse after treatment with topical steroids.

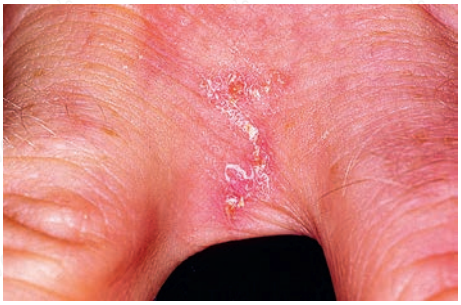

Fig. 12.8 Scabies. Small pruritic vesicles and crusted macules in the finger web spaces, which is a characteristic location to find active scabies lesions.

Fig. 12.9 Large and small, scaly, oval, pink patches in later stages of scabies infestation of the plantar feet, some with dry peripheral scale and other lesions with small hemorrhagic erosions.

Fig. 12.10 Scabies. Small, pinpoint, intensely pruritic vesicles scattered over the dorsal hand, which may be misdiagnosed as contact allergy or hand eczema.

Fig. 12.11 Scabies. Numerous scattered pruritic vesicles surrounding the medial thighs and small erosions on the glans penis, all characteristic of scabies transmitted through direct contact during sexual intercourse.

Fig. 12.12 Generalized scabies infestation in an infant, with intense pruritus. This degree of scabies infection is usually associated with an atopic dermatitis background.

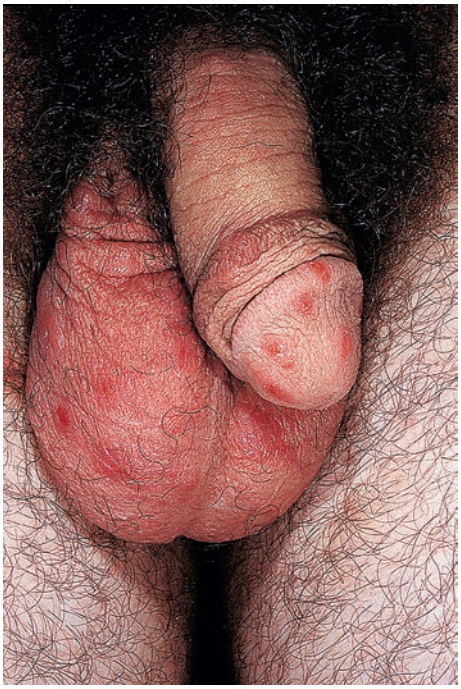

Fig. 12.13 Scabies: secondary lesions. Nodules occur in covered areas, such as the buttocks, groin, scrotum, penis, and axillae. Nodules on the penis and scrotum are highly characteristic of scabies.

Fig. 12.14 Scabies. Secondary lesions dominate the clinical picture in this case. Pustules, scaling, and erythema accompany this heavy infestation of mites.

Fig. 12.15 Scabies. Infants can develop vesicles and pustules on the palms and soles.

Fig. 12.16 Scabies. This child had an infestation for more than 3 months. Numerous, generalized lesions are present.

Lice (Pediculosis)

Description

- Lice are flattened, wingless insects that infest the hair of the scalp, body, and pubic region.
- Each variety of insect prefers a specific region of the body.
- Lice have three pairs of legs located on the anterior part of the body directly behind the head. The legs terminate in sharp claws that are adapted for feeding, permitting the louse to grasp and hold firmly onto hair or clothing.
- Lice attach to the skin and feed on human blood. They lay eggs or nits on hair shafts.
- Nits are hard, white oval lice eggs attached to the hair shaft.
- Rarely, lice can transmit disease, such as epidemic typhus and relapsing fever.
- Each type of insect is named for the area of the body which it infects:
  - Head lice infestation is caused by *Pediculus humanus* var. *capitis.*
  - Body lice infestation is caused by *P. humanus* var. *corporis.*
  - Pubic lice infestation is caused by *Pthirus pubis.*

Head Lice

- Head lice infestation is highly contagious.
- Direct contact is the primary source of transmission.
- Lice appear in the scalp hair more often in children.

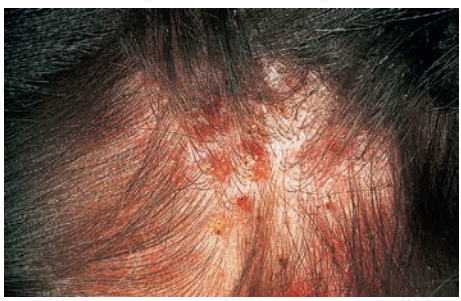

Fig. 12.17 Pediculosis capitis. Head lice are most often found in the occipital areas. Nits are deposited on the shaft about 1 mm above the scalp surface. Itching in children is often intense. It is worse at night when the lice are feeding. Excoriated lesions may become infected. Serum and crust then appear with regional lymphadenopathy.

- The insect is an obligate human parasite and thus cannot survive on other animals or furniture.
- The head louse does not carry any known human disease.
- Lice have a blood meal every 3 to 6 hours.
- They live for about 1 month.
- Females lay 7 to 10 eggs a day.
- Eggs, or nits, are firm casts cemented to the shaft, about 1 cm from the scalp surface, and hatch in 8 to 10 days.
- Additional information can be found at the website for the National Pediculosis Association (http://www.headlice.org).

History

- Head lice infestation is typically diagnosed by a schoolteacher, school nurse, or camp nurse.
- Girls are affected more often than boys.
- Fomite transmission by hats, brushes, or earphones is common.
- Infestation may cause mild itching at the nape of the neck or no symptoms at all.
- Posterior cervical adenopathy is occasionally noted.
- Infestation is rare in African American patients.
- Infestation of the eyelashes is more common in children.

Skin Findings

- Nits are small white eggs firmly cemented to the hair shafts.
- Nits are sometimes easier to see than lice.
- Head lice are 3 to 4 mm in length. They can be seen on the hair shafts and scalp with careful observation.
- Diagnosis is usually not difficult but may require repeated examinations.
- Head lice have an elongated body, similar to a body louse, though smaller.
- Honey-colored crusting or secondary impetigo and adenopathy occur if the papules become infected.
- Infestation may induce blepharitis with lid pruritus, scaling, crusting, and purulent discharge.
- Nits are fluorescent, so a Wood's light examination can be used to screen children.

Fig. 12.18 Lice: eyelash infestation. Infestation of the eyelashes is seen almost exclusively in children. It may induce blepharitis with lid pruritus, scaling, crusting, and purulent discharge.

Differential Diagnosis

- Seborrheic dermatitis
- Impetigo
- Insect bites

Treatment

Standard Topical

- Permethrin rinse 1%, an over-the-counter preparation, is often the drug of first choice for most types of lice. Shampoo and dry. Saturate hair and scalp. Rinse out in 10 minutes. An additional one or two treatments given 1 week apart may be required.
- Synergized pyrethrin shampoos and creams can be purchased over the counter. Two or three treatments given 1 week apart may be required.
- Permethrin 5% is administered for treatment failures and is left on the hair overnight under a shower cap.
- Lindane shampoo is left on the scalp and hair for 5 minutes and then washed out and repeated in 1 week.
- Malathion lotion 0.5% is rapidly pediculicidal and ovicidal. It is useful for the treatment of head lice resistant to pyrethrins and permethrin. The lotion is applied for 8 to 12 hours; it should be applied 7 to 9 days later if necessary.
- Strains resistant to permethrin and lindane have emerged in recent years.

Fig. 12.19 Body louse. Three kinds of lice infest humans. All three have similar anatomic characteristics. Each is a small (less than 2 mm), flat, wingless insect with three pairs of legs located on the anterior part of the body directly behind the head. The legs terminate in sharp claws that are adapted for feeding and permit the louse to grasp and hold firmly on to hair or clothing. The body louse is the largest of the three and is similar in shape to the head louse.

- The use of all agents should be repeated in 1 week because younger lice and nits may not be eradicated.
- Combing through hair with a special nit comb is also helpful in the week after treatment.
- Treatment of all close family members is controversial but frequently recommended.
- Headgear, clothes, brushes, combs, and bed linen are washed in hot water for 10 minutes. Articles that cannot be washed are sealed in a plastic bag for 3 days.

Alternative Therapies or "Home Remedies"

- To smother the lice, petrolatum (Vaseline), mayonnaise, or pomade is applied to the scalp overnight and covered with a shower cap.
- Copious amounts must be used to smother all lice. This treatment does not kill nits, so it should be repeated each week for 4 weeks.
- Hair Clean 1-2-3 hairspray is an oil that kills lice in 15 minutes.
- As a last resort, shaving the scalp and other affected hair-bearing areas can be curative.

Oral Treatments

- Ivermectin 200 μg/kg (typical adult dose is 12 mg as a single dose) is prescribed in a single oral dose and is repeated in 1 to 2 weeks.
- Trimethoprim–sulfamethoxazole (Bactrim, Septra) kills synergistic bacteria in lice. A prolonged course may be necessary.
- Antibiotics are administered for secondary infection, such as staphylococcal impetigo.

Nit Removal

- Removing nits is essential but difficult.
- Combing through hair with a special nit comb is also helpful in the week after topical treatment.
- Clear Lice Egg Remover gel applied to the hair and combed through removes eggs that survive lice killers.
- Hair saturated with a solution of 50% vinegar and 50% water, applied and removed in 15 minutes. may help to "unglue" nits.

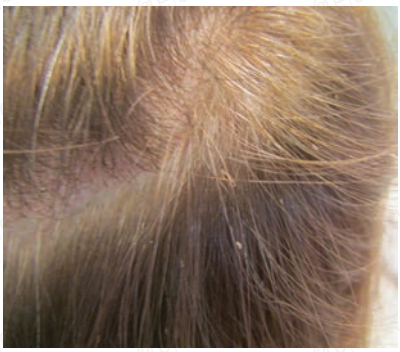

Fig. 12.21 Head louse. Nits are often visible as small, firm, white, adherent nodules on the hair shafts, which promote one to look closer for lice.

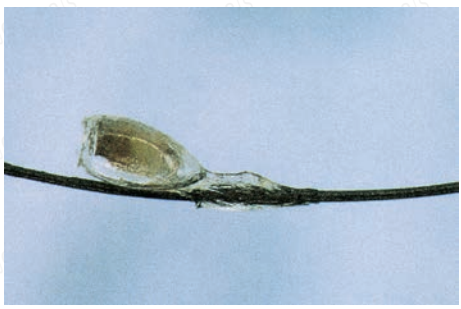

Fig. 12.20 Body louse. The louse egg (nit) is cemented to a hair shaft. It depends on body warmth to incubate and is therefore attached close to the scalp surface (about 1 cm above the scalp).

Fig. 12.22 *Pthirus pubis* (pubic or crab louse). The crab louse is the smallest louse, with a short oval body and prominent claws that resemble those of sea crabs.

Botfly Myiasis

Description

- Myiasis is an infestation of the body tissues of animals or humans by the larval stage of nonbiting flies.
- *Dermatobia hominis* causes human botfly infestation.
- This species of fly is native to Central and South America.
- The female fly uses the underbelly of mosquitoes to transmit its eggs.

History

- The human botfly larvae infestation is seen in travelers returning from Central America and South America.
- *Dermatobia* females use mosquitoes as vectors to transmit their eggs by capturing mosquitoes and depositing eggs on their bodies before releasing them.
- Fly larvae are deposited on the skin incidentally by the mosquitoes and penetrate to the subcutaneous tissue, sometimes in the mosquito bite area, where they mature into maggots.
- The larva is alive in the subcutaneous tissue and appears as an erythematous papule or nodule that can be mistaken as an inflamed cyst or furuncle.
- Within the papule is a 1- to 2-mm central punctum consisting of the breathing tube of the larva.
- Many patients report discomfort and a moving sensation within the skin.
- At maturation, the larva exits the body and drops to the ground and matures into an adult fly.

Skin Findings

- The tender red nodule is about 2 to 10 mm in diameter.
- Lesions are typically found on the scalp, face, or upper arms or chest.
- The larval breathing tube is mobile and can be seen opening and closing within the skin about once every minute.
- An inflamed cyst-like structure enlarges over days to weeks and is known as a *warble*.
- Serous or seropurulent material can be discharged from the opening.
- Unless this nodule is inspected closely, or botfly infestation is suspected, it may be misdiagnosed.
- Travel to an endemic area can aid in suspicion of the diagnosis.

Laboratory

- After extraction, the botfly larva appears as a juicy, white, pouch-like worm, with circular black spicules and with a breathing tube at one end. It is about 10 to 15 mm.
- It is important to remove or extract the entire larva because infection can occur with incomplete removal.
- There is only one larva per lesion.

Differential Diagnosis

- Inflamed or ruptured epidermal cyst
- Furuncle or abscess
- Bite reaction

Treatment

- The human botfly larva needs oxygen, so it can be forced to the surface with occlusion by the application of petroleum jelly (Vaseline) or bacitracin. In some situations, bacon fat, tape, or nail polish can be applied over the opening to deplete oxygen.
- The larva is smothered and enters the greasy trap while coming up for air. Larvae can be removed with forceps, often within 30 minutes to 3 hours after application.

Fig. 12.23 Inflamed nodule with open breathing apparatus of the botfly larvae, on the upper eyelid.

- Another technique is to inject lidocaine below the larva. The pressure may force it out of the orifice.
- On occasion the opening needs to be enlarged with a #11 blade in a cross or cruciate pattern, which allows easy extraction of the larvae.

Pearls

- The life cycle of the fly is unique, in that the female glues her eggs to the body of a mosquito or tick, which unknowingly deposits the eggs or larvae while biting or feeding.
- Most cases of botfly myiasis are suspected when recent travel to Central or South America is noted.
- Another less common type of myiasis is tungiasis, caused by the red-brown sand flea *Tunga penetrans.*
- Tungiasis is seen on the soles, toe webs, and ankles of travelers returning from Africa or Central or South America.

Fig. 12.24 *Myiasis.* **A,** A red papule 2 to 4 mm in diameter develops. An intense inflammatory reaction occurs in the tissue surrounding the larvae. **B,** Myiasis. Lesions are found on the face, scalp, chest, arms, or legs.

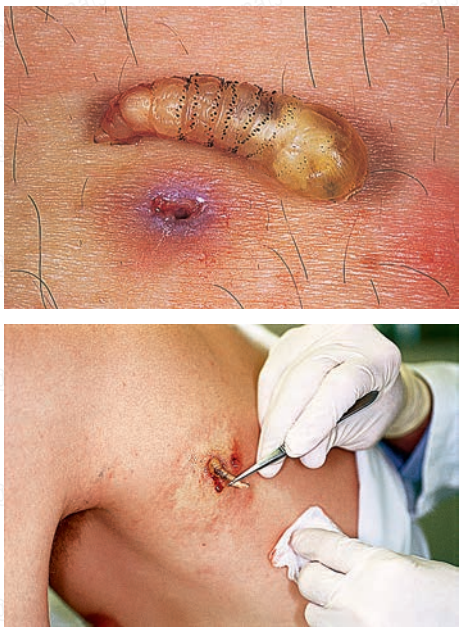

Fig. 12.25 *Myiasis.* It is usually not necessary to enlarge the hole, but in this case a #11 surgical blade was used to enlarge the hole so that this very large maggot could be extracted with forceps. Xylocaine was injected into the cavity to aid in the extraction.

Bee and Wasp Stings

Description

- Honeybees are the most common source of insect stings and can cause severe allergic reactions.
- The stinger of the honeybee separates from the bee's abdomen while stinging and remains embedded in the vertebrate's tissue.
- The stingers of other bees and wasps do not detach. The detached stinger is a useful diagnostic feature for distinguishing stings of honeybees from those of other bees and wasps.

History

- The initial sharp or painful sting lasts for a few minutes and is followed by moderate burning. Symptoms resolve in a few days.
- Most reactions in children are mild.
- Children with deeper dermal reactions still have a benign course and are unlikely to have recurrent reactions.
- Severe reactions are more common in adults.
- Localized or systemic allergic reaction may develop.
- Patients sensitized by prior stings may develop large, local reactions, with edematous swelling forming hours after the sting and resolving in a few days.
- Edema is more prominent with head and neck stings.
- A toxic systemic reaction may develop hours after the sting.
- Vomiting, diarrhea, headache, fever, muscle spasm, and loss of consciousness can occur.
- Allergic anaphylactic reactions involve itching, hives, shortness of breath, wheezing, nausea, and abdominal cramps. They occur within minutes to an hour after the sting.
- Most fatal bee and wasp stings occur in a hypersensitive person older than 40 years who has received a single sting on the head or neck. Deaths are caused by respiratory dysfunction or anaphylaxis.
- Delayed-onset allergic symptoms (up to 1 week after the sting) range from anaphylaxis to serum sickness.
- Multiple stings can cause death in nonallergic people.
- The median lethal dose of bee venom is estimated to be 500 to 1500 stings.

Skin Findings

- A hive or raised pink wheal with a central pinpoint red punctum appears minutes after the sting and lasts for about 20 minutes.
- Angioedema may occur, which is a localized reaction that appears thick, hard, and edematous over an area as large as 10 to 50 cm.

Differential Diagnosis

- Hives
- Angioedema
- Bites from other insects

Treatment

- The stinger should be removed as fast as possible. The degree of envenomation does not differ if the stinger is scraped or pinched off. A delay of just a few seconds in removing the stinger leads to greater venom delivery.
- Localized nonallergic reactions are treated with ice and cool wet dressings, whereas allergic reactions may also require antihistamines.
- Severe generalized reactions are treated with aqueous epinephrine (adrenaline) 1:1000 (0.3–0.5 mL subcutaneously), which is repeated at 20-minute intervals if needed.

Fig. 12.26 Bee and wasp stings. A large local allergic reaction larger than 10 cm in diameter.

- If the patient is hypotensive, an intravenous 1:10,000 dilution of epinephrine (adrenaline) can be administered.
- Intravenous methylprednisolone (Solu-Medrol) may be used for generalized reactions to reduce release of vasoactive compounds.
- Preloaded epinephrine (adrenaline) syringe kits are available (e.g., EpiPen Auto-Injector, Ana-Kit).
- An antihistamine (e.g., Benadryl) 25 to 50 mg can be administered orally or intramuscularly.
- Venom immunotherapy is highly effective for those with systemic reactions.

Fig. 12.27 Bee and wasp stings. A large urticarial plaque began to occur minutes after a sting. The black spot in the center is the sting site. This lesion was intensely itching and was treated with an ice-cold wet compress.

Fig. 12.28 Bee sting. Severe local reaction with necrosis and ulceration at the site of a bee sting.

Fig. 12.29 Bee sting. Huge urticarial plaque in a patient with a known history of bee-sting allergy.

Black Widow Spider Bite

Description

- The adult female of the black widow spider (*Latrodectus mactans*) is about 3 to 4 cm in length and has a shiny, fat abdomen resembling a large grape.
- The black widow spider has a characteristic red hourglass-shaped marking on the ventral surface of the abdomen.
- *L. mactans* is found from the southern United States to southern New England, but related widow spiders are found in other areas of the United States and the world.
- Systemic disease is due to the envenomation of a neurotoxin. Only the females are capable of envenomation.
- The protein component of venom (alpha-latrotoxin) causes acetylcholine depletion at motor nerve endings and catecholamine release at adrenergic nerve endings, which account for the associated symptoms.

History

- The black widow spider typically encounters humans near her web in wood or lumber piles, under a log, in a crevice of a barn, or in shoes.
- This spider is not aggressive, but envenomation occurs when the spider's environment is disturbed or when the spider is inadvertently trapped or pressed against the skin.
- The initial bite reaction may be only mildly painful.
- Abdominal pain (100%), hypertension (92%), muscle complaints (75%), a target lesion (75%), and irritability or agitation (66%) are the most common symptoms.
- Migratory muscle cramps and spasm, headache, nausea, vomiting, hypertension, weakness, tremors, paresthesias, and ultimately paralysis may occur.
- Cramping abdominal pain is common and is the classical presenting complaint; it mimics an acute surgical abdomen and occurs minutes to hours after the bite.
- Symptoms may increase in severity for up to 24 hours and then slowly subside over 2 to 7 days.
- Residual weakness, tingling, nervousness, and muscle spasms may persist for weeks to months.
- In young children or elderly people, convulsion, paralysis, and shock may occur. Death is rare.
- All symptoms are collectively known as *latrodectism.*

Skin Findings

- The clinical appearance is variable; typically, mild erythema or swelling occurs at the bite site.
- Red-brown fang marks may be seen.
- The nodes draining the bite site may become painful and enlarged.

Differential Diagnosis

- Brown recluse spider bite
- Acute surgical abdomen

Treatment

- Ice should be applied to restrict the spread of venom.
- Antivenom is used for severe envenomations with pain refractory to opioid analgesics and sedative–hypnotics (e.g., lorazepam). Antivenin (*L. mactans*) for acute symptoms is given intramuscularly or intravenously. It may also be useful days (up to 90 hours) after a bite for patients with persistent symptoms (e.g., weakness, muscle cramping, orthostatic tachycardia, increased blood pressure). The severity of symptoms usually abates within 3 hours after treatment. Occasionally retreatment is indicated. Administer in a controlled environment because severe allergic reactions are possible.
- Pain is relieved with oral or intravenous opioids and benzodiazepines.
- Muscle relaxants, such as diazepam (Valium) and methocarbamol (Robaxin), may also help.

Pearls

- Patients report spider bites, especially from black widow and brown recluse spiders, much more often than they actually occur.
- When they do occur, it is the constellation of symptoms that is needed to make the clinical diagnosis.
- Laboratory tests and biopsy are not helpful in confirming this diagnosis.

Fig. 12.30 Black widow. Only the adult females are capable of envenomation. They have a total body length of 4 cm, with a smooth black body, a globose abdomen that resembles an old-fashioned shoe button, long slender legs, and a red hourglass marking on the underside of the abdomen. Black widow spiders place their webs close to the ground in protected places near logs and in dark, sheltered areas, such as crevices in old barns, lumber piles, and privies. They usually do not bite when away from the web because they are clumsy and need the web for support.

Fig. 12.31 Black widow. Severe muscle pain is an early sign of envenomation. Pain begins in muscles near the bite site and then occurs in large groups. Cramps and muscle contractions can occur in any muscle groups but are most severe in the abdomen. The pain can mimic appendicitis.

Brown Recluse Spider Bite

Description

- The bite of the brown recluse spider (*Loxosceles reclusa*) may cause necrotic or dermonecrotic arachnidism.
- The spider is yellow, tan, or brown in color and can be identified by a dark brown, violin-shaped marking on its cephalothorax (hence the name the *fiddle-back spider*).
- The body length is 10 to 15 mm, and the leg span is about 25 mm.
- The brown recluse spider is a shy, nocturnal, nonaggressive arachnid.
- It lives in dark areas, such as woodpiles, under rocks, or in dark corners of attics, garages, or basements.
- Most are located in the south central United States.

History

- Humans come in contact with the spider accidentally.
- The bite frequently goes unnoticed.
- Localized pain, burning, and stinging occur at the bite site 6 to 8 hours later as vasospasm causes local tissue ischemia.
- Systemic symptoms—including fever, chills, nausea, vomiting, weakness, joint and muscle pain—are uncommon; they occur 12 to 24 hours after the bite and are not related to the extent of the local reaction.
- Sphingomyelinase D is cytotoxic and hemolytic and is the toxin responsible for the necrosis.
- Death is rare; most patients respond well to treatment.

Skin Findings

- The bite site may show a localized hive-like reaction with minimal redness and swelling early in the course.
- Some 10% of cases go on to develop significant skin necrosis.
- A cyanotic color, followed by expanding necrosis of the skin, develops within days.
- The most severe reaction occurs in fatty areas, such as the thighs, abdomen, and buttocks.
- The dermonecrosis can be deep and ultimately leaves an ulcer that takes weeks to months to heal.
- Upper airway obstruction has been reported in brown recluse bites on the neck.

Laboratory and Pathology

- Histology depends on the time the biopsy is taken.
- Early in the course, neutrophils are present, followed by "mummified" coagulative

Fig. 12.32 Brown recluse spider bite. A solitary, large painful indurated and hemorrhagic plaque with central punctum and necrosis, characteristic of a spider bite, which may go on to become more necrotic centrally and eventually slough.

Fig. 12.33 The brown recluse spider *Loxosceles reclusa* (fiddle-back spider) is small, the body approximately 15 mm long. Its color ranges from yellow or tan to dark brown.

necrosis of the epidermis, adnexae, and dermis.
- Vasculitis may occur in larger vessels, which resembles polyarteritis nodosa, and accounts for the dermonecrosis.

Differential Diagnosis

- Cellulitis and infection
- Ecthyma gangrenosum
- Necrotizing vasculitis
- Necrotizing fasciitis
- Pyoderma gangrenosum
- Polyarteritis nodosa

Treatment

- Most bites heal with supportive care alone.
- Treat mild localized reactions with ice, cold wet dressings, elevation, and mild analgesics. The cold limits the activity of sphingomyelinase D.
- Necrotic skin needs local wound and ulcer care. Surgical débridement is not usually needed.
- Antibiotics and tetanus toxoid are given when indicated.
- Dapsone 50 to 100 mg/day taken orally may be helpful in preventing severe necrosis.
- The use of systemic steroids is controversial.

Pearls

- A high degree of suspicion is needed to make the diagnosis of brown recluse spider bite.
- Brown recluse spider bites can produce a dramatic dermonecrotic reaction that can be confused with other systemic diseases.

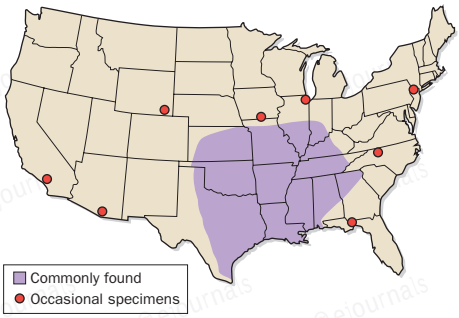

Fig. 12.34 Distribution of brown recluse spider *(Loxosceles reclusa)* in the United States.

Fig. 12.35 Brown recluse spider. A characteristic, dark, violin-shaped or fiddle-shaped marking is located on the spider's back. The broad base of the violin is near the head, and the violin's stem points toward the abdomen.

Lyme Disease

Description

- Lyme disease is a tick-borne disease caused by the spirochete *Borrelia burgdorferi.*
- *Borrelia* evolves through three stages and can affect almost all organ systems.
- The cutaneous eruption of Lyme disease is called *erythema migrans*.
- In Europe there are different species of *Borrelia* that cause Lyme disease.

History

- Lyme disease affects many organ systems, occurs in stages, and mimics several other diseases.
- Disease onset is 3 to 28 days after an infective tick bite.
- The three stages may overlap or occur alone.
- Stage 1: there is an expanding target-like patch (erythema migrans) and influenza-like symptoms occur, including fever, headache, and arthralgias.
- Stage 2: there are cardiac and neurologic system problems.
- Stage 3: arthritis and continuous chronic neurologic problems persist.

Skin Findings

- The initial tick bite inflicts a local inflamed bite reaction. The bite may be painless and go unnoticed.
- The tick must stay attached for at least 24 hours for infection to occur.
- Skin changes (erythema migrans is the most characteristic) are not present in all cases.
- Erythema migrans is a bright-red expanding eruption occurring at the site of *Borrelia* inoculation.
- It begins as a small papule with a slowly enlarging ring of erythema, which fades in 2 to 3 weeks, leaving a normal to light-blue surface.
- The erythematous patch remains flat, blanches with pressure, and (rarely) develops vesicles. It may reach up to 10 cm or more in diameter.
- The expanding border of erythema migrans may be slightly raised.
- Approximately 20% to 50% of patients have multiple concentric rings at sites of subsequent hematogenous dissemination.

Laboratory

- Diagnosis of Lyme disease without clinical confirmation of erythema migrans is difficult.
- Routine laboratory studies are not helpful.
- Serologic testing is the only practical laboratory method of diagnosing Lyme disease, but insensitivity and interlaboratory variability are frequent problems.
- The results of serologic testing for anti-*Borrelia* antibodies by enzyme-linked immunoassay are positive at the initial presentation in 25% of infected patients and are positive in 75% of infected patients 4 to 6 weeks later, even with antibiotic therapy.
- The more specific Western immunoblot test is used to corroborate equivocal or positive results obtained with the enzyme-linked immunoassay.
- High titers of immunoglobulin G or immunoglobulin M indicate disease, but lower titers can be misleading.
- A culture of *B. burgdorferi* is possible with tissue biopsy on modified Barbour–Stoenner–Kelly medium, but this is not practical.

Differential Diagnosis

- Urticaria
- Tinea
- Insect bites
- Granuloma annulare
- Cellulitis
- Fixed drug eruption

Treatment

- Preventing tick bites is the first line of defense.
- The patient should wear protective garments, tuck the pants into the socks, and wear closed-toed shoes.
- *N,N*-diethyl-metatoluamide can be used on the skin, or permethrin can be used on the clothing.
- Ticks should be detected and removed as soon as possible.
- A number of special instruments for tick removal (e.g., Ticked Off) are available.
- Adults with early Lyme disease should receive 21 days of treatment with doxycycline 100 mg twice a day, amoxicillin

Fig. 12.36 Erythema migrans: bull's-eye lesion.

Fig. 12.37 Lyme disease. A simple plastic tool called Ticked Off removes ticks, including the mouth parts. These inexpensive tools are generally available.

500 mg three times a day, or cefuroxime axetil (Ceftin) 500 mg twice a day.

- Amoxicillin 30 mg/kg per day in divided doses or cefuroxime axetil 250 mg twice a day are used for children under 8 years of age.
- Disease that has progressed to stage 2 or stage 3 may require more intensive treatment.
- Within 72 hours of discovering a deer tick that is obviously engorged, or that has been attached for more than 72 hours, on an adult from an area where Lyme disease is endemic, administer 200 mg of doxycycline as a single dose.
- Within 72 hours of discovering a deer tick, within unknown *Borrelia* carriage, that has been attached for 36 to 72 hours, consider 200 mg of doxycycline as a single dose.
- When a tick has been attached for less than 36 hours, it is not necessary to treat the bite; however, some patients and physicians may prefer to treat prophylactically anyway.
- In children, the dosage and efficacy of prophylactic treatment have not been evaluated.
- Guidelines for the management of asymptomatic patients with elevated Lyme disease titers have not been established.

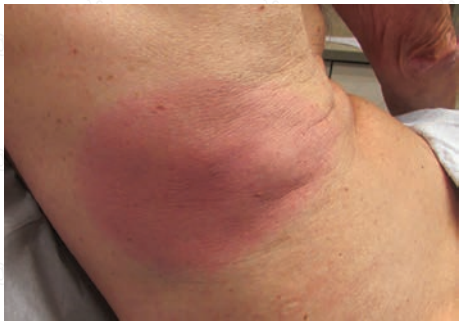

Fig. 12.38 Large erythema migrans lesion expanding symmetrically.

Fig. 12.39 Lyme disease. The most common configuration of the lesion is circular, but as migration proceeds over skinfolds, distortions of the configuration occur. Multiple lesions may occur.

Fig. 12.40 Lyme disease. Multiple, large and small, pink, round macules with central bluish hue over the trunk have a target-like appearance, characteristic of disseminated *Borrelia* infection. A central punctum is not always present, multiple lesions can be seen and can be asymptomatic, but patients with this many erythema migrans lesions usually are febrile and feel ill.

Rocky Mountain Spotted Fever

Description

- Rocky Mountain spotted fever is a potentially lethal disease caused by *Rickettsia rickettsii.*
- The infection is characterized by an acute onset of fever, a severe headache, myalgia, vomiting, and a petechial rash.
- It is transmitted by ticks, usually either *Dermacentor* or *Ixodes* species.
- Organisms disseminate through the bloodstream and multiply in vascular endothelial cells.
- This condition occurs most commonly in the south central and southeastern United States and Brazil, in the summer and early fall.

History

- The bite of a tick is typically painless, so the patient may not recall a recent tick bite.
- Travel to an endemic area and recent outdoor activity are helpful clues.
- The incubation period is on average 6 to 8 days after the bite.
- Abrupt onset of fever (95%), severe headache (90%), myalgia (85%), and vomiting (60%) occurs.

Skin Findings

- The skin findings evolve and appear a few days after the fever. Signs of previous tick bite may not be found.
- The rash is discrete and macular, blanches with pressure, and becomes petechial in 2 to 4 days.
- It appears first on the wrists and ankles, which is characteristic.
- Hours later, the rash involves the palms and soles (75%) and then becomes generalized.
- The rash does not occur at all in about 15% of cases. Rashless or spotless disease is much more common in adults.

Nonskin Findings

- Multiple organs can be involved in severe disease.
- Hepatosplenomegaly is present in 25% to 50% of cases.
- Neurologic symptoms include seizures, meningitis, cranial nerve palsies, and paraparesis.
- Respiratory distress, abdominal pain, diarrhea, severe myalgia, myocarditis, retinal thrombosis, and edema on the dorsum on the hands and feet may occur.

Course and Prognosis

- The fever subsides in 2 to 3 weeks, and the rash fades with residual postinflammatory hyperpigmentation.
- The mortality rate is 4% in treated patients and 20% in untreated patients.
- Many of those who die have a fulminant course and are dead in 1 week.

Laboratory

- The diagnosis must rely on clinical criteria (fever, rash, headache, myalgia) and tick exposure because laboratory confirmation cannot occur before 7 to 14 days after the onset of illness.
- Histology has limited use in diagnosis; Giemsa stain is used but not always accurate at identifying organisms in vessels.
- Indirect fluorescent antibody tests on acute and convalescent sera are fairly accurate and can be used to confirm the diagnosis.
- Serologic evidence appears in the second week of infection. A titer greater than 1:128 is required.
- The leukocyte count can be high, low, or normal; thrombocytopenia, an elevated serum hepatic aminotransferase level, and hyponatremia are common.

Fig. 12.41 Multiple diffuse, pinpoint, asymptomatic petichiae scattered over the hands (and feet) is a presenting sign of Rocky Mountain spotted fever, but meningococcemia must also be considered.

Differential Diagnosis

- Meningococcemia
- Mononucleosis, measles, and other viral exanthems
- Parvovirus B19 (gloves and socks variant)
- Drug eruptions
- Toxic shock syndrome
- Typhoid fever
- Vasculitis
- Kawasaki syndrome

Treatment

- Empiric treatment should be started if Rocky Mountain spotted fever is suspected.
- Doxycycline 100 mg twice a day for at least 7 days and at least 48 hours after resolution of fever is the current treatment of choice.
- Doxycycline is the most favorable agent for children younger than 9 years.
- Up to five courses of doxycycline may be administered with minimal risk for dental staining.
- Chloramphenicol 50 to 75 mg/kg/day is an alternative.

Fig. 12.42 Rocky Mountain spotted fever. The rash is reported in 83% of cases and typically begins on the fourth day, erupting first on the wrists and ankles. Within hours it involves the palms and soles (73%), and then it becomes generalized. The rash is discrete and macular and blanches with pressure at first; it becomes petechial in 2 to 4 days.

Pearls

- Petechial rash of the wrists and ankles, followed by involvement of the palms and soles, is characteristic.
- A therapeutic trial of doxycycline or tetracycline should be considered for any adult who has been in an endemic geographic area during the summer months and who has fever, myalgia, and headache and who is suspected of having Rocky Mountain spotted fever.

Fig. 12.43 Rocky Mountain spotted fever. A generalized petechial eruption that involves the entire cutaneous surface, including the palms and soles.

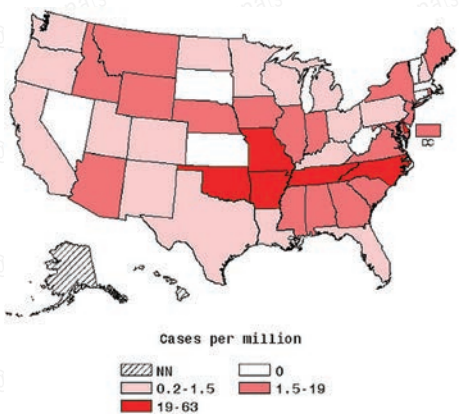

Fig. 12.44 Reported cases of Rocky Mountain spotted fever (2010) in the United States. (Courtesy of the Centers for Disease Control and Infection; http://www.cdc.gov.)

Flea Bites

Description

- The typical skin changes of flea bites are red to purpuric pruritic papules on the lower legs.
- Contact within an infested home or a vacant dwelling is also common.

History

- Clusters of pruritic red or purpuric papules develop on the legs. They can also be grouped around the ankles and waistline.
- Pants and socks offer some protection.
- This is a self-limited, itchy eruption. Depending on the patient's sensitivity, it may subside in days to weeks.
- Flea eggs can lie dormant for more than 1 year and can reactivate with vibrations from footsteps.

Skin Findings

- Initially, tiny red dots or bite puncta may be seen, often grouped around the ankles and lower legs.
- Red, raised urticarial lesions known as *papular urticaria* develop in hypersensitive patients, especially children.
- Pruritus can be intense in hypersensitive patients.
- Occasionally a pink to red halo develops around the papule.
- The persistent scratching can lead to round, white scars after healing.
- Diagnosis is usually not difficult.

Description

- The flea itself is a very small, red-brown, hard-bodied, wingless insect.
- It is flattened laterally so that it can squeeze between the hairs of its host.
- The insect is small and can be difficult to see unless inspected closely.

Treatment

- The bites are treated symptomatically.
- Topical steroids and antipruritics, such as topical steroids and Sarna lotion, can help.
- Secondarily infected lesions require antibiotics.
- Mild to moderately potent topical steroids are useful for treating intense itching and papular urticaria.
- Fleas must be eradicated. Infested animals, animal bedding, and rugs must be treated.

Fig. 12.45 Flea bites in a child were excoriated and became infected. These lesions will heal with scars.

Fig. 12.46 Fleas are tiny red-brown, hard-bodied, wingless insects that are capable of jumping approximately 60 cm. They have distinctive, laterally flattened abdomens that allow them to slip between the hairs of their host. They live in rugs and on the bodies of animals, and they may jump onto humans.

Fig. 12.47 Flea bites occur in a cluster or group.

Fig. 12.48 Flea bites are typically clustered about the lower leg. Fleas jump but cannot reach higher than above the calf. Children scratch bites, which causes them to persist and become infected.

Cutaneous Larva Migrans (Creeping Eruptions)

Description

- Cutaneous larva migrans is a migratory infestation of the skin by hookworm larvae.
- *Ancylostoma braziliense* is the most common species in North America.
- "Creeping eruption" is another name for this condition because it causes an inflamed, serpiginous pruritic eruption.
- It is the most common tropical acquired dermatosis.
- It is considered a travelers disease.

History

- The lesions typically begin about 3 weeks after a beach vacation in the Caribbean, Africa, South America, Southeast Asia, or even the southeastern United States.
- Infection can also occur in children who play in sandboxes and in carpenters and plumbers who work under houses.
- The eggs of the hookworm are passed from animal feces into warm soils or sand, where the larvae hatch.
- The larvae feed on soil, molt, and may come in contact with human skin and penetrate through follicles or fissures, causing the skin eruption.
- The hookworm larvae are indiscriminate, and the parasite can penetrate the skin when humans walk on moist feces-contaminated sand.
- A pruritic, inflammatory, serpiginous lesion that migrates in a snake-like fashion is characteristic.
- If untreated, the larvae die in 2 to 8 weeks, but persistence up to 1 year has been reported.
- The larvae are eventually sloughed away as the epidermis matures.
- Typically the resolution of migration and itching occurs within 2 to 3 days after therapy has begun.
- It may take about 1 week for the more intense allergic inflammatory response to resolve.

Skin Findings

- A local pruritic inflammatory response to the larval secretions occurs within 3 weeks of infection, usually after the traveler has returned home.
- A serpiginous red to purple lesion with a 3-mm wide tract is characteristic.
- Feet and ankles are most commonly involved, followed by buttocks, genitals, and hands.
- Itching is moderate to intense, and secondary infection and eczematous inflammation can sometimes occur.
- The worm migrates about 2 cm daily.

Nonskin Findings

- Loeffler's syndrome is a possible complication of *A. braziliense* infection and includes patchy lung infiltration and eosinophilia.

Laboratory and Testing

- Diagnosis is usually based on history and clinical examination.
- Eosinophilia, up to 30% eosinophil count elevation, has been reported and can help support the diagnosis.
- Chest radiograph may show a patchy infiltration of Loeffler's syndrome.

Treatment

- Freezing of the leading edge of the lesion with liquid nitrogen is often ineffective but can be attempted as a first-line therapy.

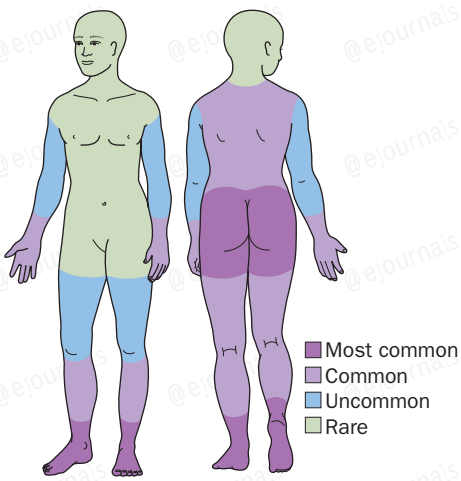

Fig. 12.49 Cutaneous larva migrans distribution diagram.

- Ivermectin 200 mcg/kg (average dose 12 mg) administered as a single oral dose is effective.
- Lesions heal within 5 days after starting ivermectin. A second round of treatment with the same dose is given for relapses.
- Albendazole (either 400 mg per day orally or 200 mg orally twice a day for 7 days) is effective and well tolerated. Its action is rapid, pruritus disappears in 3 to 5 days, and cutaneous lesions disappear after 6 to 7 days of treatment.
- Thiabendazole 15% in a liquid or a cream compound is applied topically three times a day for 5 days. It is applied to affected areas and 2 cm beyond the leading edge because the parasite is often located beyond the clinical lesion. The preparation is often difficult to obtain.
- Antibiotics are used for secondary infection.
- Topical or systemic steroids may be needed to treat severe pruritus.
- Typically, the resolution of migration and itching occurs within 2 to 3 days after therapy has begun.
- It may take a week or so for the more intense allergic inflammatory response to resolve.

Fig. 12.50 Cutaneous larva migrans. The trapped larva struggles a few millimeters to a few centimeters each day laterally through the epidermis in a random fashion, creating a tract reminiscent of the trail of a sea snail wandering aimlessly over the sand at low tide.

Fig. 12.51 Cutaneous larva migrans. The 1-cm larva stays concealed directly ahead of the advancing tip of the wavy, twisted red to purple 3-mm tract. Any skin surface can be affected.

Fig. 12.52 Cutaneous larva migrans. Many larvae may be present in the same area, creating several closely approximated wavy lines.

Fig. 12.53 Cutaneous larva migrans. During larval migration, a local inflammatory response is provoked by the release of larval secretions. Itching is moderate to intense, and secondary infection or eczematous inflammation occurs.

Fire Ant Stings

Description

- Fire ants are wingless *Hymenoptera* species.
- They were imported from South America and are now established primarily in the southeastern United States.
- Imported fire ants are small, yellow to red or black insects with large heads.
- They have prominent mandibles that grasp the victim and drive the stinger within the tail by arching the body.
- They form large colonies with giant mounds, are highly mobile, and are difficult to eradicate.
- Sting reactions range from local pustules and large, late-phase responses to life-threatening anaphylaxis.

History

- Initially burning and sharp pain occur at the sting site. A single ant can inflict multiple stings. The ant either runs across the skin, leaving a line of stings, or rotates around the point of mandible attachment, leaving a ring of stings.
- Children who are unaware of the danger are common victims, often receiving stings on their ankles and legs.
- An infestation of buildings with fire ants may be associated with indoor attacks.
- A systemic allergic reaction can occur, occasionally resulting in death from anaphylactic shock.
- Anaphylactic shock has been reported to happen with just one sting.

Skin Findings

- The classic lesion is two pinpoint red papules (the bite) surrounded by a ring of pustules (the sting).
- Edema and itching are accompanied by a wheal of 5 to 10 mm. Sterile vesicles form in about 4 hours, evolve into pustules in 24 hours, resolve in 3 to 10 days, and can leave a scar.
- Occasionally there is a large local late-phase reaction resulting in a red, edematous, indurated, pruritic plaque, which resolves in 24 to 72 hours.

Laboratory

- Skin testing is the most common method for diagnosing allergy.
- A venom enzyme-linked immunoassay can confirm fire ant hypersensitivity.
- Imported fire ant venom-specific immunoglobulin E antibodies can be measured by radioallergosorbent assay (RAST) in patients suspected of allergic reactions.

Differential Diagnosis

- Other insect bites
- Folliculitis

Treatment

- Cool wet dressings are helpful for comfort.
- Topical antipruritics (Sarna lotion) and oral antihistamines are usually all that are needed.
- A short course of prednisone is used only for severe local reactions.
- Immunotherapy should be considered for severe cases.

Fig. 12.54 Fire ant stings. Small yellow-red to black insect, with large head with inward curving jaws. The stinger is located on the tail of the ant.

Fig. 12.55 Multiple 1- to 2-mm inflamed pustules of a fire ant attack.

Fig. 12.56 Fire ant stings. Numerous pustules occurred after a child was attacked by a large colony of ants.

Swimmer's Itch

Description

- Swimmer's itch is a pruritic inflammatory response to the larval form of nonhuman schistosome parasites obtained while swimming in fresh-water lakes.
- The diagnosis is often missed when this condition occurs sporadically, because of its nonspecific characteristics.
- The eruption occurs in areas not covered by the swimming suit.
- It is frequently confused with sea-bather's eruption, which occurs in areas under the swimming suit.

History

- Indiscriminate larvae (cercariae) released from snails seek out a warm-blooded host, such as a bird, especially ducks and geese, or a rodent, such as muskrats and beavers, but may accidentally penetrate human skin.
- The parasites migrate from snails to the birds and rodents, then are rereleased in the infected feces and eggs.
- The larvae are restricted primarily to fresh-water lakes and ponds.
- This condition occurs worldwide, but the Great Lakes area has the highest incidence in the United States.
- Cercariae die after penetration into the skin, resulting in an inflammatory skin reaction.
- The intensity of the eruption depends on the degree of sensitization.
- Initial symptoms are minor after the first exposure.
- Papules occur the after the initial sensitization, approximately 5 to 15 days after the penetration.
- A typical eruption occurs with subsequent exposures.
- The eruption begins when the fresh water evaporates and cercariae begin penetrating into the skin.
- Pruritus and rash reach maximal intensity in 2 to 3 days and subside without treatment in 2 to 3 weeks.

Skin Findings

- Itching begins in approximately 1 hour after swimming.
- It is followed hours later by discrete, highly pruritic, red, edematous, bite-like papules.
- Occasionally pustules are surrounded by erythema.
- A highly sensitive person may develop secondary urticaria, vesicles, and eczematous plaques.
- The most characteristic feature is the location of the eruption, involving areas not covered by the swimming suit.

Differential Diagnosis

- Sea-bather's eruption (occurs beneath the bathing suit) after swimming in salt water
- "Hot tub" (*Pseudomonas*) folliculitis occurs after hot tub, spa, or swimming pool exposure
- Drug rash
- Eczema and atopic dermatitis

Treatment

- The eruption is self-limited.
- Symptoms should be relieved as the eruption fades.
- Itching is controlled with antihistamines and cool wet dressings.
- Intense inflammation is suppressed with medium-potency topical steroids.
- Antibiotics may be administered for secondary infection.
- Immediate towel drying might be effective if the eruption is anticipated because most larvae penetrate the skin as water is evaporating.

Fig. 12.57 Swimmer's itch. Red to pink, edematous barely raised, pruritic macules that appear in exposed areas of the skin (not beneath the bathing suit) a few hours after a fresh-water swim.

Animal and Human Bites

History

- The type of animal and the animal's behavior should be determined.
- The patient's health status, such as immunosuppression, should be known.
- Cats have long, sharp teeth that often puncture and sometimes penetrate down to tendon and bone.
- Dogs typically cause a crushing-type wound and can also cause puncture wounds and lacerations.
- Of the approximately 5 million animal bites per year in the United States, 80% are from dogs, 15% from cats, 2% to 3% from rodents, and the rest from small animals, farm animals, monkeys, and reptiles.
- Rabies transmission should be considered in the unprovoked attack of a wild animal or an unvaccinated domestic animal.
- Besides dogs and cats, bites from foxes, raccoons, skunks (Fig. 12.58), and bats are more likely to be linked to rabies.
- Seemingly trivial bites can result in infections and severe complications.
- Approximately 10 to 20 people in the United States, usually young children, die annually from dog bites.
- Human bites from an infant or child must be distinguished from those from an adult, which may be due to child abuse.

Physical Examination and Skin Findings

- The bite site should be checked for depth and underlying soft tissue and tendon injury.
- Tendon, bone, and nerve function should be tested, as well as vessel integrity.
- Crush injury is more common in animal bites.
- Body cavities and joints should be evaluated for penetration.
- Pain, erythema, purulence, and swelling suggest infection, including cellulitis and fasciitis.
- Human bites from adults can be identified by the width of the dental arch, which is greater than that of toddlers (4 cm).

Laboratory and Testing

- *Pasteurella* species are the most common isolates from dog and cat bites.
- Infected wounds should be cultured for aerobic and anaerobic organisms.
- Cultures taken at the time of injury may be of little value.
- Crush injuries, suspected fractures, and foreign body penetrations should be examined radiographically.

Treatment

- Antibiotics are used to treat and prevent infection.

Fig. 12.58 Large symmetric and hemorrhagic erosions and puncture wounds from a canine bite.

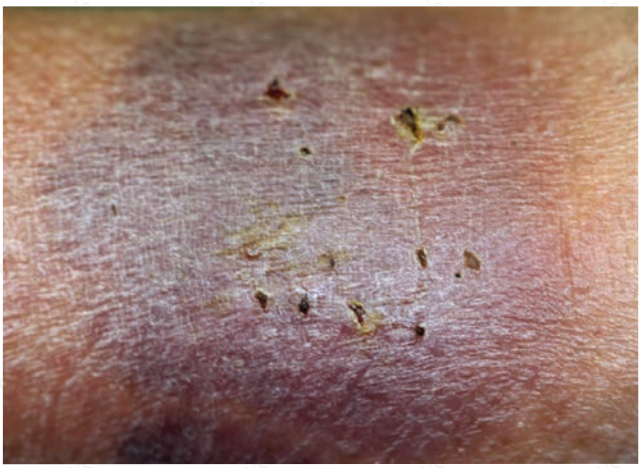

Fig. 12.59 Purpuric patch surrounding bite and claw marks after a skunk bite on the ankle.

Fig. 12.60 Symmetric hemorrhagic and purpuric erosions consistent with human bites.

- Cat bites with a deep puncture, wounds that require débridement, and contaminated wounds are routinely treated with antibiotics.
- Asplenic, immunocompromised elderly patients and those with diabetes are routinely treated with antibiotics.
- Empirical therapy for dog bites and cat bites should be directed against *Pasteurella* organisms, streptococci, staphylococci, and anaerobes.
- Empiric treatment of dog and cat bites is similar. Cat bites have a greater prevalence of anaerobes and *Pasteurella multocida.* Oral amoxicillin–clavulanate (3–7 days) is recommended first-line treatment for animal and human bites. Alternative oral agents include doxycycline, or penicillin VK plus dicloxacillin. Other options, including fluoroquinolones, trimethoprim–sulfametho xazole, and cefuroxime, may require an additional agent active against anaerobes, such as metronidazole or clindamycin. First-generation cephalosporins—such as cephalexin, penicillinase-resistant penicillins (e.g., dicloxacillin), macrolides (e.g., erythromycin), and clindamycin—all have poor in vitro activity against *P. multocida* and should be avoided for animal bites.
- When given alone, azithromycin or trovafloxacin may also be useful.
- The decision whether to close the wound is made based on the increased risk for infection versus the functional and cosmetic benefits.

- Facial lacerations from dog or cat bites are usually closed.
- Clean wounds, or those that can be easily cleansed, are sutured immediately.
- Rabies infection is the other major consideration when dealing with animal bites.
- Wounds are irrigated with normal saline or povidone–iodine 1% solution at high pressure. Cleaning a bite with soap is as effective as cleaning with quaternary ammonium compounds in lowering the risk for transmission of rabies.
- A healthy-appearing animal should be confined and observed for 10 days.
- Any animal that behaves wildly or erratically after biting a person should be destroyed and examined histologically for rabies.
- Rabies prophylaxis is indicated if the laboratory evaluation finds that the animal was rabid or if the animal was not captured.
- Patients not previously vaccinated are given both human rabies vaccine (a series of five doses administered in the deltoid area) and rabies immune globulin (20 international units/kg). As much as possible of the rabies immune globulin should be infiltrated in and around the wound, and the remainder should be given intramuscularly at a site distant from that used for vaccine administration.
- Vaccination is prophylactic; when signs of rabies occur, the chance of survival is diminished.
- Tetanus immune globulin and tetanus toxoid are given to patients who have two or fewer primary immunizations.
- Tetanus toxoid alone is given to those who have completed a primary immunization series but who have not received a booster for more than 5 years.

Vesicular and Bullous Diseases 13

James G. H. Dinulos

Dermatitis Herpetiformis

Description

- Dermatitis herpetiformis (DH) is a chronic pruritic vesicular rash commonly occurring on the extensor surfaces and is a manifestation of gluten sensitivity.

History

- In adults, DH is twice as common in males.
- In children, females are more commonly affected.
- Most patients with DH are of northern European descent.
- DH rarely occurs in Asians and Africans.

Skin Findings

- Severe, unremitting itching and burning are a constant feature. The classical rash consists of clustered vesicles symmetrically distributed on the elbows, knees, sacrum, and base of the scalp.
- Intact vesicles are often destroyed by scratching and are often difficult to identify.
- Patients may also develop nonspecific papules, urticaria, hemorrhagic macules, and erosions.
- Rarely, the rash may be limited to the face.
- Oral lesions are uncommon.

Nonskin Findings

- Ninety percent of patients have gluten-sensitive enteropathy.
- The severity of skin disease does not correlate with degree of intestinal involvement.
- DH is associated with thyroid disease (e.g., Hashimoto's thyroiditis) and enteropathy-associated lymphoma.
- Enteropathy-associated lymphoma risk is reduced with a gluten-restricted diet.

Laboratory

- Skin biopsies should be performed for standard histology and direct immunofluorescence.
- Immunoglobulin A (IgA) deposits are found in the dermal papillae in 90% of cases.
- Circulating IgA antiendomysial antibodies are found in the serum of 70% of patients, not on a gluten-free diet.
- Serum IgA antiendomysial antibody titers correlate with severity of jejunal villous atrophy.
- Serum IgA level and IgA antitransglutaminase-2 antibodies should be ordered in patients with suspected DH.
- If IgA antitransglutaminase-2 antibodies are increased, then antiendomysial antibodies should be ordered.

Course and Prognosis

- DH is a chronic condition with spontaneous remission in 30% of people.
- Systemic iodides may aggravate DH.

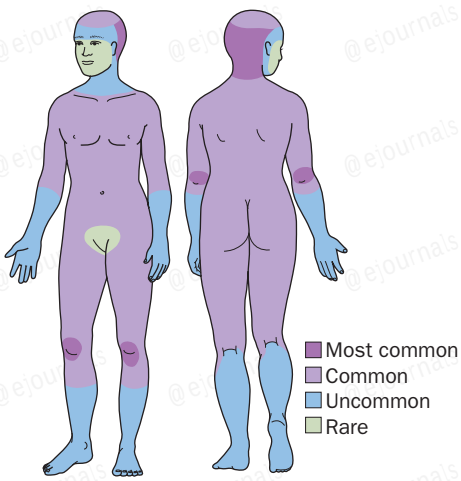

Fig. 13.1 Dermatitis herpetiformis distribution diagram.

Fig. 13.2 Dermatitis herpetiformis. The vesicles are symmetrically distributed and appear on the elbows, knees, scalp and nuchal area, shoulders, and buttocks. The distribution may be more generalized.

Fig. 13.3 Dermatitis herpetiformis. Vesicles appear singly or in clusters and resemble herpes simplex. Patients scratch the vesicles to relieve itching; therefore, it is often difficult to find an intact lesion to biopsy.

Fig. 13.4 Dermatitis herpetiformis. "Herpetiform" refers to the typical grouping of vesicles.

Fig. 13.5 Dermatitis herpetiformis. Intact vesicles with surrounding inflammation sprinkled among erosions and excoriations.

Fig. 13.6 Dermatitis herpetiformis. Classical distribution of dermatitis herpetiformis with excoriated lesions on the elbows and buttocks.

- DH is recurrent but usually is well controlled with oral sulfones, such as dapsone, or a strict gluten-free diet.

Differential Diagnosis

- Arthropod bite
- Scabies (when excoriated, is also intensely itchy; look for burrows)
- Atopic dermatitis
- Lichen simplex chronicus

Treatment

- A gluten-free diet can control DH and allow decreased requirement for oral medication.
- Gluten is a protein found in wheat, rye, and barley.
- Rice, oats, and corn do not contain gluten.
- Treatment does alter severity of symptoms, but does not alter disease duration.
- Oral dapsone 100 to 150 mg every day is the drug of choice and typically relieves itching and burning within 48 to 72 hours.
- Daily maintenance dose of dapsone varies from 25 to 200 mg per day.
- Obtain a pretreatment glucose-6-phosphate dehydrogenase level. Patients with low levels are at increased risk for hemolysis.
- Sulfapyridine 500 to 1500 mg per day is effective in some patients as an alternative to dapsone.
- Tetracycline 500 mg one to four times per day, minocycline 100 mg twice a day, and nicotinamide 500 mg two to three times a day have been reported to be helpful in some cases.

Pearls

- Intense unremitting itch, unresponsive to prednisone, suggests scabies or DH.
- Immunofluorescence confirms the diagnosis of DH.
- Although DH is a blistering disease, bullae are rarely seen; pruritus induces scratching, and removes vesicles and small bullae, leaving only crusted papules and small erosions.

Fig. 13.7 Symmetric distribution of vesicles in dermatitis herpetiformis.

Fig. 13.8 Dermatitis herpetiformis. More widespread involvement may result in vesicles and bullae. Bullous impetigo and bullous pemphigoid would also be diagnostic considerations.

Pemphigus Vulgaris

Description

- Pemphigus vulgaris is a rare, life-threatening, autoimmune, intraepidermal blistering disease, involving the skin and mucous membranes.

History

- The mean age of onset is 60 years.
- There is no gender predilection.
- Incidence is estimated at 0.5 to 3.2 cases per million.
- Incidence is highest in people of Ashkenazi Jewish descent in association with human leukocyte antigens HLA-DR4 and HLA-DQ8, and in non-Jewish patients in association with human leukocyte antigens HLA-DR6 and HLA-DQ5.
- Oral erosions usually precede the onset of skin blisters by weeks or months.
- Itching is minimal; most patients describe skin tenderness or irritation.

Skin Findings

- Bullae vary from 1 to 3 cm or larger in diameter.
- They appear gradually and may be localized for a considerable length of time, but become generalized if untreated.
- Bullae rupture easily.
- Applying pressure to small, intact bullae causes the fluid to dissect laterally into the midepidermal areas altered by bound IgG (Asboe–Hansen sign).
- Traction pressure on intact skin causes bullae formation (Nikolsky's sign).
- Erosions last for weeks before healing with brown hyperpigmentation.
- Painful oral erosions occur in 50% to 70% of patients and typically precede the skin blisters by weeks or months.
- Blisters, erosions, and lines of erythema may appear in the pharynx and esophagus.

Laboratory

- Skin biopsy shows intraepidermal bulla, acantholysis (separation of epidermal cells), and a mild to moderate infiltrate of eosinophils.
- Direct immunofluorescence is performed on two biopsies: one from the edge of a fresh lesion, and a second from an adjacent normal area.
- IgG and often complement C3 are found in the intercellular substance areas of the epidermis.
- Indirect immunofluorescence confirms circulating serum IgG antibodies in 80% to 90% of patients with active disease.
- Antibodies are directed against desmoglein-3, an intracellular keratinocyte adhesion molecule.
- The level of antibody reflects the activity of disease and requires monitoring.
- Periodic serum tests to detect changes in titers are helpful in evaluating the clinical course.

Course and Prognosis

- In the past, death occurred in nearly all cases, usually from cutaneous infection.
- With modern treatment, death occurs in only 5% to 15% of cases and is usually from complications of steroid therapy.
- Patient comorbidities, such as osteoporosis, diabetes, and hypertension, contribute to mortality risk.

Differential Diagnosis

- Pemphigus foliaceus and paraneoplastic pemphigus (neoplasia-associated pemphigus)

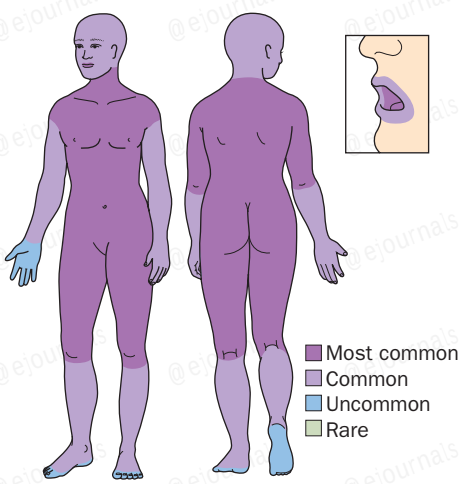

Fig. 13.9 Pemphigus vulgaris distribution diagram.

Treatment

- Treatment is very complicated and best accomplished with the help of experts.
- The goal of treatment is to arrest blister formation and maintain the skin barrier.
- Prednisone with an immunosuppressive adjuvant agent, such as azathioprine or mycophenolate mofetil, is standard treatment.
- Adjuvant drugs have a "steroid-sparing" effect.
- Therapeutic choices are affected by the patient's age and degree of disease involvement.
- Starting dosages of prednisone typically vary between 40 and 120 mg/day and are subsequently tapered to establish a minimum dose that controls most disease activity.
- Mycophenolate mofetil or azathioprine is initiated with or after starting corticosteroids.
- Intravenous immune globulin, pulse-dose intravenous corticosteroids, dapsone, and intralesional steroids may be more effective for selected patients than the previously discussed regimens.
- Direct immunofluorescence should be performed before therapy is discontinued.
- A negative direct immunofluorescence finding is a good indicator of remission.
- Rituximab may induce remission.

Pearls

- Pemphigus vulgaris may present with only oral lesions.
- Early cutaneous findings of pemphigus vulgaris may resemble bullous pemphigoid and other immunobullous diseases.
- Strongly consider dermatology referral for suspected cases because both diagnosis and management require specialist training.

Fig. 13.11 Pemphigus vulgaris. Large irregular moist erosions among intact flaccid bullae.

Fig. 13.10 Pemphigus vulgaris. Isolated painful oral erosions may be the first presentation of pemphigus.

Fig. 13.12 Oral erosions usually precede the onset of skin blisters by weeks or months.

Fig. 13.13 Pemphigus vulgaris. Flaccid blisters rupture easily because the roof consists only of a thin portion of the upper epidermis and is very fragile. Healing is with brown pigmentation but without scarring.

Fig. 13.14 Pemphigus vegetans is a localized variant of pemphigus vulgaris involving the mouth and inguinal region and is due to antibodies against desmoglein-3.

Fig. 13.15 Pemphigus vulgaris. Flaccid blisters rupture easily. Widespread cutaneous involvement places the patient at risk for sepsis because of the compromised skin barrier. Patients with severe disease should be treated similar to burn patients.

Pemphigus Foliaceus

Description

- Pemphigus foliaceus is an autoimmune, intraepidermal blistering disease characterized by crusted patches and erosions.
- Blister location is more superficial in the epidermis compared with pemphigus vulgaris.

History

- The age of onset varies more widely than in pemphigus vulgaris.
- It occurs in middle-aged and older people.
- There is no racial predilection.
- Pain and burning are more often reported than itching.
- Sun or heat may worsen the signs and symptoms.
- Pemphigus foliaceus has been reported in approximately 5% of patients taking D-penicillamine or captopril.

Skin Findings

- Lesions appear in a "seborrheic distribution" on the face or first appear on the scalp, chest, or upper back.
- Intact blisters are not usually seen.
- The vesicle roof is so thin that it ruptures, and serum leaks out and desiccates, forming localized or broad areas of crust.
- If present, intact thin-walled blisters are sometimes seen near the edge of the erosions.
- The upper portion of the epidermis can be dislodged with lateral pressure.

Nonskin Findings

- There is increased incidence of thymoma, myasthenia gravis, and other autoimmune disease.

Laboratory

- Skin biopsy shows an intraepidermal bulla or acantholysis (separation of epidermal cells) in the upper epidermis and mild to moderate infiltration of eosinophils.
- Direct immunofluorescence is performed on two biopsies: one from the edge of a fresh lesion, and the second from an adjacent normal area.
- IgG and often complement C3 are found in the intercellular substance areas of the epidermis.
- Indirect immunofluorescence on serum confirms circulating IgG antibodies in approximately 75% of patients with active disease.
- Antibodies are directed against desmoglein-1, an intracellular keratinocyte adhesion molecule.
- The level of antibody reflects the activity of disease.

Differential Diagnosis

- Lesions are well demarcated and do not extend into large eroded areas as those of pemphigus vulgaris
- Impetigo may appear similar to pemphigus foliaceus
- Seborrheic dermatitis

Course and Prognosis

- May be localized for years or progress rapidly and become generalized evolving into an exfoliative erythroderma.
- May last for years and may be fatal if not treated.

Treatment

- Early localized disease may be managed with groups I to III topical steroids.
- Active widespread disease is treated like pemphigus vulgaris.
- Rituximab may induce remission.

Pearls

- Early pemphigus foliaceus may resemble seborrheic dermatitis or other papulosquamous diseases.

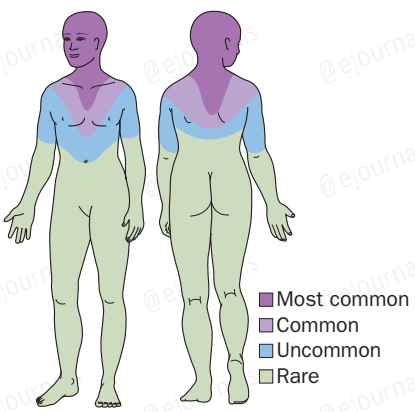

Fig. 13.16 Pemphigus foliaceus distribution diagram.

Bullous Pemphigoid

Description

- Bullous pemphigoid is the most common autoimmune, subepidermal blistering disease of the skin.

History

- Bullous pemphigoid primarily affects elderly people, with most cases occurring after age 60.
- Childhood cases have been reported but are extremely rare.
- There is no racial or gender prevalence.
- IgG autoantibodies directed against hemidesmosomal proteins are present.
- The trigger factor for the formation of autoreactive antibodies is unknown.
- Drugs, including furosemide, captopril, and some nonsteroidal anti-inflammatory drugs, have been implicated.

Skin Findings

- The eruption is usually generalized with a predilection for skinfolds, flexural areas, and dependent areas.
- Bullous pemphigoid starts with a localized area of erythema or with pruritic urticarial papules, coalescing into plaques.
- A diagnosis of hives is frequently made in this preblistering (urticarial) stage.
- Plaques turn dark red in 1 to 3 weeks as vesicles and bullae rapidly appear on their surface.
- Itching is usually moderate to severe.
- The bullae are tense with good structural integrity.
- Firm pressure on the blister will not result in extension into normal skin as occurs in pemphigus. Traction on normal skin will not produce bullae.
- Bullae rupture within 1 week, leaving an eroded base, which heals rapidly.

Nonskin Findings

- Peripheral blood eosinophilia occurs in some patients.
- Oral blisters, if present, are mild and transient.

Laboratory

- Skin biopsy shows subepidermal bulla with an infiltrate of eosinophils within the dermis and blister cavity.
- Direct immunofluorescence of skin sampled next to a blister confirms IgG and/or complement C3 in a linear band at the basement membrane zone in about 90% of cases.
- IgG autoantibodies may be directed against one of two hemidesmosomal proteins BPag1 (230 kd) or, less often, BPag2 (180 kd).
- Direct immunofluorescence studies may be useful in following response to treatment.
- As the disease subsides, complement C3 deposits disappear.
- Indirect immunofluorescence will demonstrate circulating IgG antibodies in the serum of approximately 70% of patients.
- Circulating autoantibody titers do not correlate with disease activity.

Differential Diagnosis

- Pemphigus vulgaris
- Dermatitis herpetiformis
- Bullous drug eruptions
- Epidermolysis bullosa acquisita
- Cicatricial pemphigoid

Course and Prognosis

- Untreated bullous pemphigoid may remain localized, undergo spontaneous remission, or rapidly generalize.
- Recurrences are usually less severe than the initial episode.
- Duration varies from 9 weeks to 17 years.
- The remission rate is 30% at 2 years and 50% at 3 years.
- Late relapse is observed after disease-free intervals of more than 5 years.
- Mortality rate at 1 year is 19%, often from treatment side effects in addition to patient comorbidities.

Treatment

- The goal of treatment is to arrest blistering, decrease itching, maintain the skin barrier, and limit secondary infection.
- Itching is controlled with hydroxyzine 10 to 50 mg every 4 hours as needed. Hydroxyzine causes sedation. Use with caution in elderly people.
- Class I topical steroids (clobetasol) may be used to control limited or regional disease, applied twice daily until lesions are healed.

- Minocycline, tetracycline, or erythromycin may be effective.
- Niacinamide 1.5 to 2.5 g/day may be effective.
- Some 40% of patients (especially patients with biopsies showing increased neutrophils) respond to dapsone 100 mg/day.
- Methotrexate 10 mg/week is effective to treat bullous pemphigoid.
- Prednisone 1 to 1.5 mg/kg/day is used until blistering ceases. Most patients are controlled in 28 days, and the dosage can be gradually tapered.
- Consider adjuvant immunosuppressive therapy with mycophenolate mofetil or azathioprine.
- Intravenous immune globulin therapy has been used for patients unresponsive to conventional immunosuppressive treatment.
- Rituximab induces remission in select patients.

Pearls

- Sustained remission requires gradual taper of prednisone and other agents.

Fig. 13.17 Pemphigus foliaceus. **A,** The disease begins gradually on the face in a "butterfly" distribution, or it first appears on the scalp, chest, or upper back as localized or broad continuous areas of erythema, scaling, crusting, or occasionally bullae. **B,** The roof of the vesicle is so thin that it ruptures. Serum leaks out and desiccates, forming localized or broad areas of crust. Intact thin-walled blisters are sometimes seen near the edge of the erosions.

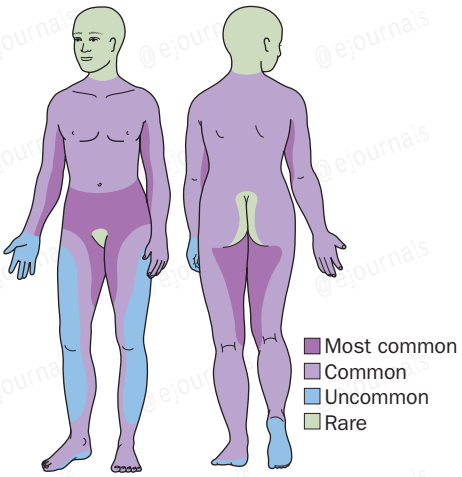

Fig. 13.18 Bullous pemphigoid distribution diagram.

Fig. 13.19 Bullous pemphigoid. Pemphigoid begins with a localized area of erythema or with pruritic urticarial plaques that gradually become more edematous and extensive.

Fig. 13.20 Bullous pemphigoid. The eruption is often generalized, but the most common sites are the lower part of the abdomen, the groin, and the flexor surfaces of the arms and legs. The palms and soles are affected. The plaques turn dark red or cyanotic in 1 to 3 weeks, resembling erythema multiforme, as vesicles and bullae rapidly appear on their surface.

Fig. 13.21 Bullosa diabeacorum. This disease does not occur on an erythematous base, like bullous pemphigoid.

14 Connective Tissue Diseases

Kathryn A. Zug

Lupus Erythematosus

General Description

- Cutaneous lupus erythematosus is a disease with a wide spectrum of manifestations ranging from solitary chronic skin lesions in chronic cutaneous lupus erythematosus (CCLE), to widespread polymorphous lesions in subacute cutaneous lupus erythematosus (SCLE), to multiple-organ involvement in systemic lupus erythematosus (SLE). Lupus is thought to be a dysregulation of T cells causing the activation of B cells, producing a variety of autoantibodies directed against cellular antigens, such as DNA, RNA, and RNA–protein complexes.
- Beware of drug-induced lupus variants; the clinical manifestations and serum findings are similar to idiopathic lupus. These variants include drug-induced SLE, SCLE, and CCLE. Drugs most frequently associated with drug-induced SLE are hydralazine, procainamide, isoniazid, methyldopa, chlorpromazine, quinidine, and minocycline. Drug-induced SLE usually spares kidneys and the central nervous system.

Treatment Overview

- Review drug associations and, when possible, remove suspect medications that may be triggers of disease.
- Sunscreen use and sun avoidance behavior are an essential element of therapy.
- Sunscreens should be used that block broad-spectrum ultraviolet A—especially ones that contain Mexoryl SX (ecamsule) or Mexoryl XL or titanium dioxide and zinc oxide.
- Excellent broad-spectrum sunscreens are Anthelios XL SPF 60 (La Roche–Posay) or Ombrelle SPF 60 sun cream (L'Oreal).
- Sun-protective clothing is available from Sun Precautions (2815 Wetmore Avenue, Everett, WA 98201; Tel: 1–800–882–7860; http://sunprecautions.com), Coolibar (http://www.coolibar.com), and from many other vendors.
- Vitamin D should be supplemented because patients are likely to have low vitamin D levels from sun avoidance.
- Smoking cessation should be encouraged because better disease control may be achieved. Less response to treatment is seen in smokers.
- There are many treatment options. Whether to use a topical agent alone or with the addition of a systemic agent depends on the degree of disease extent and severity and other individual underlying medical conditions.
- Newer immune modulators, pimecrolimus cream (Elidel) or tacrolimus ointment (Protopic), can be effective adjunctive therapy. Both are applied twice daily to

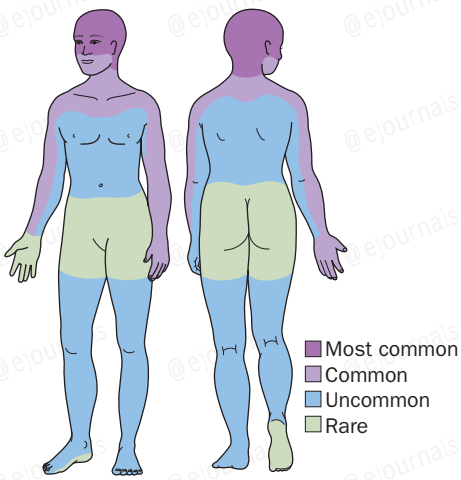

Fig. 14.1 Lupus erythematosus distribution diagram.

lesional skin for extended periods and may be preferred first-line topical therapy for facial lesions.
- Topical or intralesional corticosteroids, retinoids, and oral antimalarial therapy are standard treatments.
- Cyclical use of groups I and II topical steroids; these are administered twice a day for 2 weeks, and moisturizers are used for 1 week.
- Steroids, such as triamcinolone (Kenalog) 10 mg/mL, are injected into CCLE lesions.

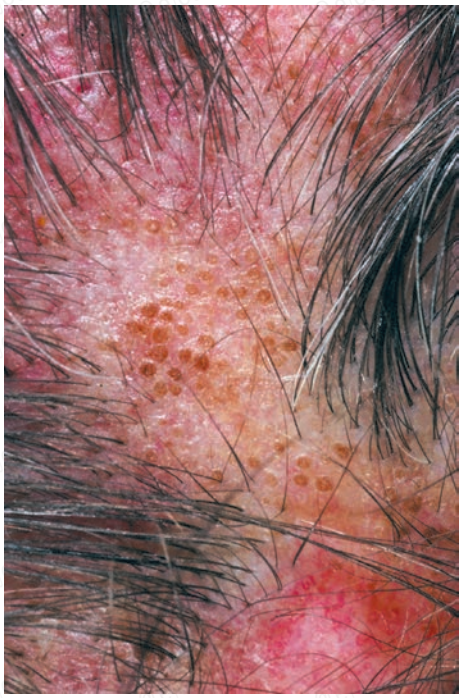

Fig. 14.2 Chronic cutaneous lupus (discoid lupus) of the scalp. Hyperkeratosis and inflammation occur. Older lesions scar and show follicular plugs. Keratin accumulates and dilates the follicular orifice causing the follicular plugging.

- Corticosteroid-impregnated tape (Cordran tape) is an option for CCLE lesions.
- Hydroxychloroquine 200 to 400 mg once daily (dose less than 6.5 mg/kg once daily) is an effective first-line oral treatment in most cases; the onset of effect requires 4 to 8 weeks. Ophthalmic examinations are required at baseline and every 6 months to 1 year. Quinacrine can be added for resistant disease at a dose of 50 to 100 mg/day.
- Other medications for cutaneous lupus erythematosus that may be considered include dapsone 25 to 200 mg twice daily (especially useful for bullous lupus erythematosus, vasculitic lesions of lupus erythematosus, or urticarial vasculitis associated with SCLE, and oral ulcerations); thalidomide in divided doses of 50 to 300 mg a day; sulfasalazine divided doses of 1.5 to 2 g/day; retinoids (e.g., acitretin 10 to 50 mg once daily or isotretinoin 1 mg/kg once daily). Prednisone 0.5 to 1.5 mg/kg once daily is an option, but long-term treatment should be avoided. Steroid-sparing immunosuppressive options include azathioprine (1–2.5 mg/kg/day); methotrexate (up to 20 mg once a week); mycophenolate mofetil (500–1000 mg twice daily); or cyclophosphamide.
- High-dose intravenous immune globulin (IVIG) 1 g/kg once daily for two consecutive days a month can be used when other agents fail; treatment is expensive, and response duration is limited.
- Rituximab alone or in combination therapy has been successful in treating patients with severe refractory cutaneous lupus erythematosus.
- Skin disease often occurs with systemic disease in patients with SLE. Such patients require systemic immunosuppressive therapy to treat this form of lupus.

Fig. 14.3 Lupus erythematosus. Erythematous patch on the malar region most typically spares the nasolabial fold and nose. Malar rash is specific for acute cutaneous lupus erythematous and is present in 20% to 60% of patients with lupus.

Fig. 14.4 Lupus erythematosus. Pink erythematous macules coalescing on the proximal interphalangeal joints and dorsum of the hands. These areas of involvement support suspicion of photo-distribution.

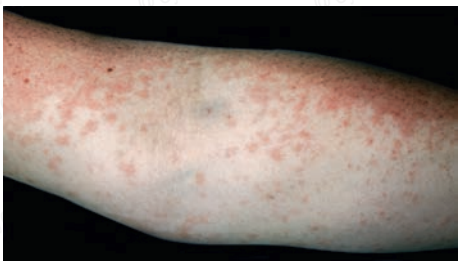

Fig. 14.5 Erythematous coalescing macules scattered on the forearm of a patient with systemic lupus erythematosus.

Fig. 14.6 Multiple atrophic macules on the dorsum of the hands in a patient with generalized discoid lupus erythematosus. The lesions of chronic cutaneous lupus are scarring.

Fig. 14.7 Violaceous macules scattered on the palms of this patient with systemic lupus erythematosus.

Chronic Cutaneous Lupus Erythematosus

Description

- CCLE is the most common form of cutaneous lupus erythematosus; lesions may be localized to the head and neck or widespread and consist of scaling erythematous papules and plaques, often with central atrophy and scarring.
- CCLE lesions are not always "discoid," and this term should no longer be used.

History

- CCLE is more common in women.
- It is perhaps more common in people with an African American background.
- The peak incidence is in the fourth decade.
- Trauma and ultraviolet light may initiate and exacerbate lesions.
- Photosensitivity is present in 50% of patients with lupus erythematosus.
- There is a lower incidence of systemic disease; 1% to 5% of cases progress to SLE. Patients with nonlocalized, widespread disease are at greater risk for advancing to systemic disease.
- Scarring alopecia is permanent.
- Drug-induced CCLE is rare and may be provoked by tumor necrosis factor (TNF)-alpha inhibitors.
- Pediatric discoid lupus erythematosus (DLE) is uncommon but is associated with SLE when lesions are generalized.

Laboratory

- Antinuclear antibodies (ANAs) are positive in only 20% of cases; anti-Ro antibody is very uncommon.
- Assess for SLE with a complete blood count, urinalysis (proteinure higher than 3), antinuclear antibody, erythrocyte sedimentation rate. If ANA is positive, then assess for extractable nuclear antibodies (double-stranded DNA, SS-A/SS-B, anti-Smith antibody, antiphospholipid antibody).
- Skin biopsy shows an interface dermatitis with follicular plugging, perivascular and periappendeal infiltrate, and possibly scarring.

Skin Findings

- Lesions may occur on any body surface, but the scalp, face, and ears are the most common areas.
- Chronic lupus erythematosus begins asymptomatically; there are well-defined, elevated, red to violaceous, 1- to 2-cm, flat-topped plaques with firmly adherent scaling.
- Follicular plugs are prominent; peeling the scale reveals an undersurface that looks like a carpet penetrated by several carpet tacks.
- Epidermal atrophy gives the surface either a smooth white or wrinkled appearance.
- Lesions may be hypertrophic or verrucous; they may involve the palms and soles or the oral mucosa.
- Lesions endure for months; they either resolve spontaneously or progress with further atrophy, ultimately forming smooth, white or hyperpigmented, depressed scars with telangiectasia and scarring alopecia.
- Scalp disease begins with erythema, scaling, and follicular plugging.
- Hair follicles are destroyed, resulting in irreversible, scarring alopecia. Hair loss is haphazard in distribution.
- Drug-induced CCLE may have classical discoid lesions or lupus tumidus lesions. An ANA test is positive in two thirds of cases.

Treatment

- Initial treatment options include groups I to III topical steroids (i.e., fluocinonide cream 0.05%), intralesional steroids, antimalarials (e.g., hydroxychloroquine 200 mg twice daily), or acitretin 25 to 50 mg/day. Hydroxychloroquine and acitretin work equally well, but acitretin has more side effects and is more costly. Other alternative treatments include dapsone and oral corticosteroids. Difficult cases can be treated with methotrexate, azathioprine, thalidomide, or isotretinoin. IVIG may be tried in recalcitrant disease. Sunscreens are an essential aspect of therapy. Some patients may respond to tacrolimus ointment (Protopic). A broad-spectrum, water-resistant sunscreen should be applied daily (see treatment overview).

Fig. 14.8 Round, erythematous plaques with depressed scarred areas surround the mouth in this patient with discoid lupus. Treatment is essential to prevent the scaring from these lesions.

Fig. 14.9 Plaques of chronic cutaneous lupus, which are both erythematous and hyperpigmented, are oval with central scaling. Biopsy confirms the diagnosis.

Fig. 14.10 Chronic cutaneous lupus. The face is the most commonly affected area. Epidermal atrophy occurs early and gives the surface either a smooth, white appearance or a wrinkled appearance.

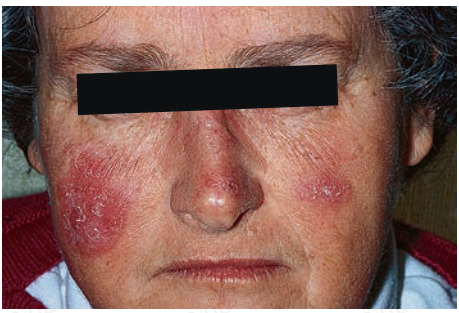

Fig. 14.11 Chronic cutaneous lupus. Red plaques and scale are seen; scarring has not yet occurred.

Fig. 14.12 Classical discoid lupus lesions showing atrophic scarring in the center, whereas surrounding the scarred areas remain actively inflamed.

Fig. 14.13 Subtle pink scaling plaque on the medial cheek. Look for follicular plugging. There may be prior scarred lesions. A biopsy was consistent with chronic cutaneous lupus.

Subacute Cutaneous Lupus Erythematosus

Description

- SCLE is a form of cutaneous lupus erythematosus typically characterized by nonscarring, erythematous psoriasiform lesions or annular lesions in a sun-exposed distribution.
- It is most common in white, young to middle-aged women.

History

- Often a sudden eruption occurs after sun exposure, but this gradually progresses to involve more skin over time.
- Lesions occur on the upper trunk, nape of the neck, upper back and shoulders, extensor arms, face, and dorsal hands.
- Internal involvement is limited and less severe than in SLE; it may not be notable at all.
- Individual lesions may last for months.
- This condition tends to be chronic and recurrent, with flaring during spring and summer months or during times of high sun exposure.
- Drug-associated SCLE is the most common drug-induced lupus variant. Patients are often older than patients with idiopathic SCLE. It is similar to idiopathic SCLE clinically and serologicially but more frequently also involves the legs, and may have a bullous presentation. Arthritis, serositis, or major organ involvement is usually absent. Development ranges from 4 to 20 weeks after drug initiation. Some medications associated with SCLE include calcium channel blockers, angiotensin-converting enzyme inhibitors, thiazide diuretics, terbinafine, statins, tamoxifen, proton pump inhibitors, the antidepressant bupropion, the nonsteroidal anti-inflammatory drugs piroxicam and naproxen, interferon-beta, leflunomide, docetaxel, and anti-TNF medications.

Skin Findings

- There are two patterns: papulosquamous and annular polycyclic. The annular polycyclic lesions may have little scaling.
- Lesions occur most often on the sun-exposed trunk; they are rarely seen below the waist.
- Subtle gray hypopigmentation and telangiectasia are seen in the center of annular lesions; this becomes more obvious as lesions resolve. Hypopigmentation fades in several months, but the telangiectasia persists.
- Follicular plugging, adherent hyperkeratosis, scarring, and dermal atrophy are not prominent features; these are more typical of discoid lesions.
- Other signs include photosensitivity in 70% to 90%, periungual telangiectasia, CCLE, and necrotizing vasculitis.
- Other variants of SCLE are neonatal lupus erythematosus, complement C2–deficient lupus erythematosus–like syndrome, drug-induced SCLE, and tumid lupus.

Laboratory

- The ANA titer is elevated in 50% to 72% of cases.
- Anti-Ro (anti–SS-A) antibody titer is elevated in 50% to 100% of cases. Patients with Ro/SS-A antibodies are at increased risk for new autoimmune diseases and drug-induced SCLE.
- Anti-La (anti–SS-B) is positive in fewer patients; it most frequently coexists with anti-Ro (anti–SS-A) and is usually not present as a unique antibody.
- Leukopenia is present in 25% to 50% of patients with SCLE.

Differential Diagnosis

- Drug eruptions, or drug-induced lupus
- Dermatomyositis
- Secondary syphilis
- Psoriasis
- Cutaneous T-cell lymphoma
- Seborrheic dermatitis
- Tinea corporis

Discussion

- Patients with SCLE do not meet criteria for SLE, although involvement is not strictly cutaneous; some have renal or

neurologic involvement and other systemic manifestations, such as fatigue and arthralgia. Hematologic involvement with leukopenia, decreased complement levels, and lymphopenia may also occur. The overall prognosis is better for SCLE than for lupus erythematosus.

- Mothers with Ro antibodies may transmit neonatal lupus; the incidence in one study was 7.6%.

Fig. 14.14 Papulosquamous rounded patches are scattered in a photo distribution in this patient with subacute cutaneous lupus. Drug-induced subacute cutaneous lupus erythematosus should always be considered.

Fig. 14.15 Annular and polycyclic erythematous plaques of subacute cutaneous lupus erythematosus. The border of lesions is scaly. Lesions are rare below the waist. Biopsy is helpful in distinguishing this eruption from psoriasis or cutaneous T-cell lymphoma.

Neonatal Lupus

- Neonatal lupus is acquired through transplacental maternal autoantibodies, typically to Ro/SS-A. The infant presents with cutaneous lupus lesions at birth or within days to months after birth, or congenital heart block. Thrombocytopenia is present in 10% to 20%.
- Neonatal lupus skin lesions are annular plaques with overlying fine scale; they resolve spontaneously in weeks to months and may leave residual telangiectasias, mild atrophy, or pigmentary alteration. Lesional skin biopsy shows typical lupus erythematosus changes, and Ro antibodies are present in most affected neonates and their mothers.
- Complete irreversible heart block occurs in roughly half of infants with neonatal lupus and can cause significant morbidity and mortality. A pacemaker is required for complete heart block.
- A mother of a child with neonatal lupus is at high risk for having other children similarly affected; early prenatal counseling and high-risk obstetric expertise are advised.
- Sun-protective measures, including broad-spectrum sunscreen, are an essential element of treatment for neonatal lupus. Low-potency topical steroid or the topical immune modulators tacrolimus or pimecrolimus may hasten lesion resolution.

Fig. 14.16 Neonatal lupus. Annular erythematous plaques with a slight scale usually appear on the head slightly after birth. Sun-exposed areas of the arms and trunk may also be involved. Telangiectasia is often prominent. Skin lesions resolve with time.

Acute Cutaneous Lupus Erythematosus

Description

- Acute cutaneous lupus erythematosus is a serious multisystem disease.

History

- Women are affected more often than men, in a ratio of 8:1.
- It occurs most frequently in people aged 30 to 40 years.
- Sunlight exacerbates acute cutaneous lupus erythematosus and may induce it.
- Acute cutaneous lupus erythematosus is a multisystem disease; there may be fever, arthritis, and renal, cardiac, pulmonary, and central nervous system involvement.

Skin Findings

- Superficial and indurated, nonpruritic, erythematous to violaceous discoid lesions (plaques) appear on the sun-exposed chest, shoulders, extensor arms, and backs of the hands.
- The malar rash may be painful or pruritic and is often triggered by sun exposure.
- There may be fine scaling on the surface and obvious follicular plugging.
- In 10% to 50% of patients, a butterfly rash appears over the malar and nasal bridge but spares the nasolabial folds.
- Atrophic scarring is seen in older lesions.
- Nail fold capillary microscopy reveals tortuous "meandering" capillary loops.
- The patient may have excess vellus hair at the frontal margin (lupus hair) or diffuse hair thinning.
- The patient has photosensitivity.
- Alopecia (scarring and nonscarring) occurs in 20% of cases. Alopecia may be patchy or generalized.
- Oral ulcers, usually painless, or nasopharyngeal ulcerations can occur.
- Other nonspecific findings may include urticaria, nonerosive arthritis, serositis, and neurologic disorders, such as seizures or psychosis. Panniculitis, leukocytoclastic vasculitis, Raynaud's phenomenon, mucous membrane ulcerations, and livedo reticularis have occurred.

Differential Diagnosis

- Contact dermatitis
- Rosacea
- Erysipelas
- Seborrheic dermatitis
- Tinea
- Drugs (e.g., hydralazine, procainamide, and anticonvulsants may cause a lupus-like syndrome)
- Polymorphous light eruption
- Parvovirus B19

Laboratory

- Biopsy of lesional skin is obtained for routine study and for immunofluorescence.
- Underlying systemic lupus erythematosus is screened for by using an antinuclear antibody titer, a complete blood count (leucopenia <4000/mm, lymphopenia <1500/mm, thrombopenia <100,000/mm), a serum chemistry profile, and urinalysis (proteinuria >0.5 g/day or >3 on dipstick).
- Anti–double-stranded DNA is highly specific but less sensitive than ANA; anti-Smith antibody is highly specific for SLE. If the patient has a history of livedo reticularis, arterial or venous thrombosis, or fetal demise, consider antiphospholipid antibodies (immunoglobulin G or M anticardiolipin antibodies, lupus anticoagulant).

Treatment

- Sunscreens are an essential aspect of therapy. A broad-spectrum, water-resistant sunscreen should be applied daily.
- Treatment of the systemic disease usually is also effective in minimizing the cutaneous manifestations.

Pearls

- The classic butterfly rash over the malar and nasal area occurs in 10% to 50% of patients with acute lupus erythematosus, but it is not the most common cutaneous presentation.
- Assessing the rashes of lupus erythematosus and categorizing the process as chronic cutaneous lupus, subacute cutaneous lupus, or acute lupus is vital to effective and appropriate treatment. It involves careful attention to systemic symptoms and hematologic, renal, and serologic evaluation.

Fig. 14.17 Acute lupus erythematosus. Superficial red plaques occur on sun-exposed areas. There may be fine scaling on the surface, but atrophy does not occur. Plaques last for days or weeks. Indurated plaques may last for months.

Fig. 14.18 Acute lupus erythematosus. Patches of erythema, the classic butterfly distribution with sparing of the nasal-labial fold.

Fig. 14.19 Photodistributed bright red erythematous patches. The clinical impression of lupus erythematosis is confirmed by lesional biopsy. Drug-induced lupus should also be considered.

Box 14.1 Workup for Suspected Cutaneous Lupus Erythematosus*

- History and physical examination
- Skin lesion biopsy for histologic studies
- Complete blood count, erythrocyte sedimentation rate, platelet count
- Antinuclear antibodies
  - Anti-nDNA
  - Anti-RNP (U1-RNP)
  - Anti-Ro (SS-A), anti-La (SS-B), SM, anti-SM
- Serologic tests
- Urinalysis

Optional Tests

- Serum protein electrophoresis
- Circulating immune complexes
- Immunofluorescence skin biopsy
- Antiphospholipid antibodies
- Total hemolytic complement (if abnormal, C2, C3, C4 levels)
- Creatinine clearance

*Including discoid lupus erythematosus, subacute cutaneous lupus erythematosus, and system lupus erythematosus.

Dermatomyositis

Description

- Dermatomyositis is an acquired, idiopathic connective tissue disease characterized by proximal muscle weakness and a characteristic, violaceous skin rash prominent on the eyelids, scalp, metacarpophalangeal joints, and bony prominences.
- Diagnostic criteria requires two of the following: (1) symmetric proximal muscle weakness, (2) elevated muscle enzymes, (3) abnormal electrocardiogram, (4) abnormal muscle biopsy, (5) cutaneous findings.
- The condition may be associated with underlying malignancy. Extramuscular findings include arthralgia, arthritis, Raynaud's phenomenon, interstitial lung disease, and cardiomyositis.
- Muscle weakness is not always present (dermatomyositis sine myositis).

History

- Incidence is 1 in 100,000, and females are twice as likely to develop the disease as males.
- At least 15% of cases occur in the pediatric age group.
- The disease may present with gradual onset of the typical skin findings or with a proximal muscle weakness.
- Patients with muscle disease often have difficulty combing their hair, walking up stairs, performing overhead tasks, swallowing, or getting up from a chair without the use of their arms. These are good screening questions.
- Cutaneous lesions often precede muscle involvement by 3 to 6 months.
- Drug triggers of dermatomyositis include hydroxyurea, interferon-beta, and TNF inhibitors.
- Mortality rate is roughly 10% and mainly due to the cardiac and pulmonary involvement.

Skin Findings

- About 10% of patients have characteristic skin findings without evidence of muscle disease. The term *amyopathic dermatomyositis* applies to skin disease in the absence of muscle disease over 6 months; 2 years is required for confirmed amyopathic dermatomyositis.
- The heliotrope rash refers to a violaceous erythema, with or without edema of the eyelids.
- Pathognomonic Gottron's papules are located over bony prominences, particularly the proximal interphalangeal joints, the distal interphalangeal joints, and the metacarpophalangeal joints. The lesions are violaceous papules and plaques. Other sites include the elbows, knees, lateral thighs, and medial malleoli.
- The "shawl sign" refers to the violaceous erythema over the back of the neck and posterior shoulders.
- The scalp may be scaly and pruritic; there may be diffuse hair loss.
- Poikiloderma (erythema, telangiectasia, hypopigmentation and hyperpigmentation, and atrophy) is also a typical finding in affected skin of the upper chest, posterior shoulders, buttocks, and back.
- Periungual changes include ragged cuticles, erythema, and telangiectasia.
- Scalp findings are common and include alopecia, pruritus, erythema, and scaling.
- Skin lesions are often pruritic.
- "Mechanic's hands" refers to scaly fissures and inflammatory changes of the hands bilaterally.
- Calcinosis is a rare but severe associated finding in dermatomyositis patients, particularly children.
- Gastrointestinal ulcerations and infections are more common in children.

Nonskin Findings

- Fatigue is a common complaint; patients may not recognize muscle weakness.
- Muscle involvement is typically proximal and symmetric. There may be muscle tenderness.
- Dysphagia occurs in 12% to 45%; all patients should be evaluated for esophageal dysfunction.
- Dermatomyositis may be a paraneoplastic disease; adults and older patients are at greater risk.

Laboratory

- Skin disease findings are typical and may be supported by biopsy of affected skin.
- Serum muscle enzymes are elevated. Creatine kinase, aldolase, and lactate dehydrogenase are enzymes helpful in assessing disease activity.
- A muscle biopsy may be performed; noninvasive imaging of the muscles can be done with magnetic resonance imaging.
- An abnormal electromyogram is one of the diagnostic criteria.
- Pulmonary function testing with diffusion capacity should be performed to assess for interstitial lung disease.
- Jo-1 antibody is positive in about 20% of patients. It is associated with interstitial lung disease, arthritis, Raynaud's phenomenon, and a hyperkeratotic callused appearance of the thumbs and the index and middle fingers (mechanic's hand).
- In adults older than 45 years, initial and ongoing screening for malignancy is advised with regular careful review of systems; rectal, stool guaiac, pelvic, and breast examinations; complete blood count; serum chemistry; chest radiograph; Papanicolaou or prostate-specific antigen test; and mammogram. Consider colonoscopy and computed tomography of the chest and abdomen. Other testing is done as indicated by symptoms or previous malignancy history. Screen for ovarian cancer in older women. Older white patients are at risk for ovarian, lung, gastric, colorectal, pancreatic, and breast cancer and non-Hodgkin's lymphoma.

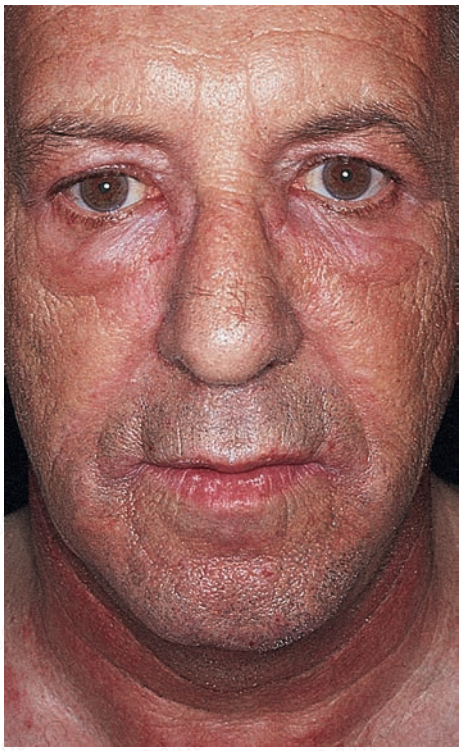

Fig. 14.20 Heliotrope rash. A violaceous to dusky-red rash involves the periorbital skin or only the lid margin. The purple skin color may be accompanied by edema. The eyelid rash is sometimes mistaken for an allergic contact dermatitis. The scalp also is often erythematous, pruritic, and scaly.

Fig. 14.21 Faint pink papules and telangiectasis on anterior neck in a patient with dermatomyositis—the "shawl sign."

Fig. 14.22 Violaceous papules over the bony prominences of the fingers are called *Gottron's papules*. They may also be found on the elbows, knees, and feet. A violaceous rash, with or without scale, may appear on the back of the hands and palms.

Fig. 14.23 Dermatomyositis: violaceous scaling patches on the face and dorsal interphalangeal joints. The knuckles are involved; they are spared in systemic lupus erythematosus.

Younger males are at risk for testicular cancer, and younger females are at risk for ovarian cancer. Patients in Southeast Asia are at risk for nasopharyngeal carcinoma.

Complications

- Untreated muscle disease can result in serious complications and chronic disability.
- Severe muscle disease may result in mortality from dysphagia, aspiration, and respiratory failure.
- Cutaneous lupus and vasculitis may overlap in some patients with dermatomyositis.

Course and Prognosis

- The disease course is variable; it may be rapid and progressive or chronic and relapsing. Spontaneous remission can also occur.
- Earlier intervention and therapy with systemic corticosteroids results in improved prognosis in patients with muscle disease.

Pediatric Considerations

- Vascular involvement is more frequent in children and may result in cutaneous ulceration.
- Joint contractures and atrophy are more common findings affecting children.
- A source of substantial disability, soft tissue calcification occurs in roughly 40% to 70% of children with dermatomyositis; treatment is difficult.
- Reduced morbidity and mortality are associated with corticosteroid treatment with or without other immunosuppression.
- Children with dermatomyositis should be treated by a specialist with particular interest in this condition.
- Malignancy is a rare association of childhood dermatomyositis.

Fig. 14.24 Dermatomyositis: heliotrope (violaceous) discoloration around the eyes and periorbital edema.

Differential Diagnosis

- Contact dermatitis
- Lupus erythematosus
- Psoriasis
- Parvovirus B19

Treatment

- Sun protection with broad-spectrum sunscreens, protective clothing, and behavior modification is necessary. The rash is often aggravated by sun exposure.
- The skin disease may be refractory to treatment, whereas the muscle disease may respond to treatment.
- Smoking cessation is recommended.
- Systemic corticosteroids (prednisone 0.5–1 mg/kg once daily) are a treatment cornerstone, although the rash may not respond. Taper slowly to half the original dose over 6 months, with the goal of stopping treatment by 2 years. If there is high muscle disease activity, start oral prednisone 1 mg/kg/day and consider adding azathioprine or methotrexate. Prednisone can begin to be tapered at 6 to 8 weeks, if muscle disease in control. Slow taper is recommended. Many patients are often able to stop corticosteroids completely between 2 and 3 years.
- Hydroxychloroquine 200 mg once to twice daily, alone or combined with quinacrine 100 to 200 mg once daily, results in improvement in the skin disease, but the response may not be complete.
- Steroid-sparing agents for skin disease include the immune-suppressive agents methotrexate 2.5 to 20 mg/week and IVIG 2 g/kg for 2 consecutive days.
- Antihistamines are used for the pruritus (nonsedating during the day or sedating at night).
- Second-line agents for muscle disease treatment and steroid-sparing include methotrexate 20 to 25 mg/week with folic acid daily, azathioprine 1.5 to 3 mg/kg/day in divided doses, cyclosporine 2 to 5 mg/kg/day in divided doses, cyclophosphamide is given IV 0.5 to 1 g/m^2 repeated monthly for 3 to 6 months, and IVIG 2 g/kg given either 1 g/kg/day for two days every 4 weeks or 0.4 mg/kg/day for five days initially and then for 3 days monthly.
- Passive range-of-motion exercise, rest, proper nutrition, and physical and occupational therapy are all important.

- Ophthalmologic screening and follow-up are essential for patients treated with hydroxychloroquine or chloroquine.

Pearls

- There is no correlation between the muscle disease involvement and activity and the skin disease.
- Amyopathic dermatomyositis is more common in adults than in children.
- Findings that favor a diagnosis of dermatomyositis rather than lupus include the characteristic violaceous hue of the cutaneous lesions, eyelid involvement, frequent pruritus, and interphalangeal joint skin involvement.
- Antimalarial myotoxicity may occur in as many as 6% of patients treated with antimalarial therapy. Consider in patients with persistent weakness and elevation of muscle enzymes.

Fig. 14.25 Periungual erythema and telangiectasia of dermatomyositis. A hand-held dermatoscope is helpful in assessment of nail folds. Scleroderma–dermatomyositis overlap syndrome has been defined as two or more of the following findings in at least two nail folds: enlarged capillary loops, capillary loss, disorganization of the normal distribution of capillaries, "budding" or "bushy" capillaries, twisted enlarged capillaries, and capillary hemorrhages.

Fig. 14.26 Calcinosis cutis is a complication of childhood dermatomyositis and can lead to secondary infection. The lesions are firm, yellowish erythematous nodules that are often tender, and secondary extrusion of calcium through the skin can result. Calcinosis is one of the expanded criteria in the diagnosis of juvenile dermatomyositis.

Scleroderma

Description

- Progressive systemic sclerosis is an idiopathic fibrosing condition that may present in a diffuse cutaneous or limited cutaneous form.
- Diffuse cutaneous systemic sclerosis by definition requires proximal involvement, can affect the entire skin surface, and is associated with internal organ fibrosis and vascular abnormalities.
- A localized variant now called *limited cutaneous systemic sclerosis* (previously CREST syndrome: *c*alcinosis, *R*aynaud's phenomenon, *e*sophageal dysmotility, *s*clerodactyly, and *t*elangiectasia).
- Limited cutaneous systemic sclerosis, which most commonly involves the hands, face, and lower legs, follows a more indolent course.

History

- Systemic sclerosis is rare; the incidence in the United States is about 20 cases per 1 million population.
- Women are affected three times more often than men.
- Peak age of onset is between ages 30 and 50 years.
- Men, older age of onset, and African American people seem to have a worse prognosis.
- The disease may remain localized on the hands for many years.

Skin Findings

- Raynaud's phenomenon may precede the onset of progressive systemic sclerosis and is often the first manifestation.
- Patients may complain of intense pruritus early in the disease.
- The modified Rodnan skin score is a validated tool to measure sclerosis.
- Early on, the affected skin is erythematous and swollen.
- Sclerosis occurs, and the skin is smooth, yellowish, and firm. It appears tight and bound down.
- Nail folds may show capillary dilatation. Dilated, tortuous capillaries are evident in 75% of patients.
- The earliest changes may be most notable around the mouth and on the hands; there is loss of the normal facial expression lines and difficulty in opening the mouth, and the lips appear thin with radial furrowing.
- Trophic ulceration and gangrene may occur on the fingertips.
- Diffuse calcification may occur within the skin and may be apparent on radiographic examination.
- Late changes include hyperpigmentation or depigmentation, often seen on the upper chest. Hair follicles will often retain pigment, whereas the adjacent skin is hypopigmented.
- Hair loss is evident in affected areas late in the disease. Alopecia may be partial or complete.

Nonskin Findings

- The limited form is associated with Raynaud's phenomenon, which may precede the sclerosis by years.
- In progressive systemic sclerosis, the heart, gastrointestinal tract, lungs, and kidneys may be affected.
- Scleroderma renal crisis typically occurs within the first 5 years of the disease. Screening with blood pressure monitoring, urinalysis, complete blood count, and creatinine at regular visits and home blood pressure monitoring are recommended.

Laboratory

- ANA patterns associated with systemic sclerosis include homogeneous, speckled, and nucleolar types. ANA positivity occurs in more than 90% of both limited and diffuse forms of cutaneous systemic sclerosis. Antibodies to Scl-70 occur in diffuse cutaneous systemic sclerosis and are associated with truncal scleroderma and pulmonary fibrosis; renal disease in this subset is less common.
- RNA polymerase III antibodies are found in diffuse cutaneous systemic sclerosis.
- Anticentromere antibody (speckled pattern) is highly specific for the limited form of cutaneous systemic sclerosis (CREST syndrome).

- The homogeneous pattern is associated with PM-Scl antibodies and is a marker for polymyositis–scleroderma overlap.
- Antibodies to single-stranded DNA are associated with linear scleroderma.
- The diffuse form of the condition has protean complications; evaluation of internal organ involvement is essential, as is assessing for musculoskeletal effects; gastrointestinal, renal, and pulmonary involvement; and pulmonary arterial hypertension.

Differential Diagnosis

- Scleroderma
- Myxedema
- Eosinophilic fasciitis (typically spares the hands and face)
- Chronic graft-versus-host disease
- Occupational exposure to chemicals (polyvinyl chloride resins, epoxy resins, silica) and chronic vibration

Complications

- Digital ulcerations and gangrene occur in roughly one third of patients.
- Asymptomatic or symptomatic esophageal dysfunction is common.
- Gastroparesis can occur.
- Interstitial lung disease and pulmonary arterial hypertension are two pulmonary complications; the lung involvement is the most common cause of death. Shortness of breath and dry cough are common presentations.
- Renal involvement affects 10% to 15% of patients. Blood pressure should be monitored regularly.

Course and Prognosis

- Progressive systemic sclerosis follows a variable and unpredictable course.
- Survival may be roughly predicted by extent of skin involvement within 1 year of diagnosis.
- The best prognosis is for patients with sclerodactyly only; truncal involvement heralds the worst prognosis, with only 21% 10-year survival.

Treatment

- There is no reliable and effective treatment to reverse or prevent the fibrosis of systemic scleroderma; the disease is typically refractory to treatment, although angiotensin-converting enzyme inhibitors are effective in the treatment of scleroderma renal crisis.

Fig. 14.27 In early disease, the hands are edematous and swollen. The edematous phase precedes the sclerotic phase. Note also the prominent facial telangiectatic mats.

Fig. 14.28 Multiple telangiectasias on the lips of a patient with limited cutaneous systemic sclerosis (CREST syndrome).

- A multidisciplinary approach to treatment is appropriate for managing the complications of this multisystem disease. Raynaud's phenomenon may be managed with behavior modification for cold avoidance, with consideration of therapy with calcium channel blockers, such as nifedipine 10 mg twice or three times daily, or amlodipine 2.5 mg once daily. Systemic immunosuppressive therapies (i.e., methotrexate or mycophenolate mofetil) have shown some success. Trials of anti-CD20 rituximab have been reported to have some success in improving skin fibrosis and pulmonary fibrosis. There are trials of autologous stem cell transplantation; allogenic bone marrow transplantation has been effective in uncontrolled trials.
- Physical and occupational therapies are important aspects of treatment.
- For skin involvement, lubrication can help relieve pruritus. Sarna lotion or Pramosone lotion 2.5% may be tried for antipruritic effect.
- Intravenous iloprost has used in the treatment of severe Raynaud's phenomenon with ulceration.
- Bosentan, the endothelial receptor antagonist, has been approved in Europe for prevention of digital ulceration.
- An interleukin-6 inhibitor (Tocilizumab) is investigational and is showing promise in treatment trials.
- Not smoking and prevention of trauma are key in the prevention of digital ulcerations; warm-water soaks for 20 minutes three times a day may be helpful. Meticulous wound care for ulceration is essential.
- Patient education materials may be obtained through the Scleroderma Foundation, 300 Rosewood Drive, Suite 105, Danvers, MA 01923 or http://www.scleroderma.org.

Fig. 14.29 Painful digital-tip ulcerations are a feature of scleroderma. Calcium is often extruded from the ulcerations.

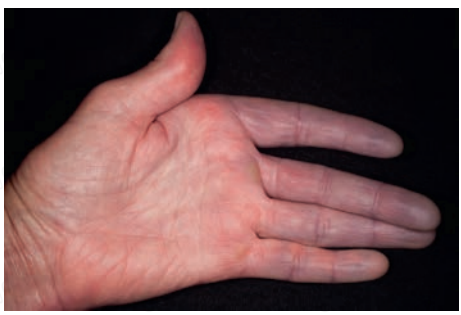

Fig. 14.30 Digital ischemia and blue fingers in a patient with Raynaud's phenomenon. The three phases of Raynaud's are (1) white—due to vasoconstriction; (2) blue—due to cyanosis, and (3) red—due to rapid blood reflow.

Fig. 14.31 Edema of the fingers is one of the first signs of systemic sclerosis. Also note the ragged cuticles and the capillary dilation.

Pearls

- Calcinosis may result in tender skin lesions and ulceration in patients with late-stage scleroderma or patients with limited cutaneous systemic sclerosis (CREST syndrome). Diltiazem may be effective in some patients.
- Smoking cessation is critical, especially in patients with Raynaud's phenomenon.
- A few patients with limited cutaneous systemic sclerosis progress to systemic disease.

Fig. 14.32 Limited cutaneous systemic sclerosis (CREST syndrome) is characterized by calcinosis, Raynaud's phenomenon, esophageal dysmotility, sclerodactyly, and telangiectasias. Note the absent forehead wrinkles, radial furrowing, and telangiectasias in this patient.

Morphea

Description

- Morphea is an idiopathic disease that manifests as sclerotic dermal plaques with violaceous borders and central hypopigmentation.
- The condition may be localized (more than two plaques) or generalized (more than three plaques).
- Depth of involvement helps determine response to treatment. Superficial involvement responds to topical treatment and phototherapy, whereas deep involvement may require systemic therapy.
- The generalized form accounts for 15% of patients with morphea.
- Linear scleroderma accounts for 20% of localized scleroderma. It is most common on the extremities but may affect the face.

History

- Morphea is more common in women than in men; the ratio is 3.6:1.
- All ages may be affected, but the mean age of onset is 32 years.
- Incidence is 27 per million per year; prevalence is about 540,000 in the United States.
- Onset may be slow and insidious or rapid and progressive.

Skin Findings

- Early lesions are typically inflammatory and, thus, violaceous. Later lesions manifest hyperpigmentation, fibrosis, and atrophy.
- In generalized morphea, a large area of skin may be involved; lesions are often truncal but may involve the extremities.
- Linear scleroderma is more common on the extremities than the face. It can impair proper growth and movement of the affected limb. It does not involve internal organs. This disease does not evolve into systemic scleroderma.
- *En coup de sabre* is the term for linear scleroderma affecting the forehead and scalp. In Parry–Romberg syndrome (progressive facial hemiatrophy), soft tissue and bony defects are also apparent.
- Examine the mouth and genitals; perform a neurologic examination if there is head and neck involvement.

Laboratory

- A skin biopsy can help confirm the clinical diagnosis; a biopsy to deep fat or fascia may be necessary if the involvement is deep. Findings include a variable degree of inflammation (typical of early lesions) and dermal sclerosis.
- Consider biopsy if not a classical presentation.
- Complete blood count and differential blood count are performed. Eosinophilia is common.
- ANA testing is positive in 50% of patients with generalized morphea.

Differential Diagnosis

- Systemic sclerosis (scleroderma)
- Nephrogenic fibrosing dermopathy
- Granuloma annulare
- Intramuscular injection reaction to drugs (vitamin K, pentazocine)
- Eosinophilic fasciitis

Course and Prognosis

- The natural history of the condition is unpredictable; lesions may spontaneously resolve after several years (3–5 years) of inflammation and enlargement.
- Although lesions may soften, hyperpigmentation is often chronic and distressing to the patient.
- Patients with generalized morphea may have asymptomatic internal organ involvement; the evaluation and proper screening of such patients is presently uncertain and individualized.

Treatment

- Because lesions may darken with sun exposure, sun protection is advised.
- Emollients may be comforting.
- Education of the patient regarding the disease may be all that is required because there is no reliable effective treatment. Reassure the patient with plaque morphea or linear morphea that this condition is benign and does not involve internal organs.
- Mid- to high-potency topical steroid cream or ointment (groups II–III) may be helpful in some cases to soften lesions and decrease pruritus. Alternately, tacrolimus ointment

twice daily can be tried for 12 weeks as a first-line agent.
- Inflammatory lesions can be injected with intralesional triamcinolone 5 to 10 mg/mL; caution is needed because intralesional steroid injection may also result in excessive atrophy.
- Calcipotriene ointment (Dovonex) twice daily can be used in adults and children; a reasonable trial of use is 8 weeks.
- Only active disease responds to immunosuppression.
- For rapidly progressing symptomatic disease, consider prednisone 20 to 40 mg once daily for 6 to 8 weeks. A taper by 10 mg every other day is appropriate for patients with lesion improvement; such treatment does not alter the natural history of the disease.
- Hydroxychloroquine 200 mg twice a day. If a response is obtained, a maintenance dose of 200 mg once daily is reasonable.
- Phototherapy with low-dose ultraviolet A, psoralen plus ultraviolet A, or ultraviolet A1 (not available in the United States) can result in improvement.
- Immune-suppressing medications, such as methotrexate or cyclosporine, may be considered for a short-term therapeutic trial of 3 to 6 months in patients with inflammatory, symptomatic, or progressive disease. Proper monitoring of such drugs is imperative.
- Patients with linear scleroderma may benefit from surgery if there are significant contractures or leg-length discrepancies. Cosmesis with autologous fat transfer can be helpful forfacial atrophy. Mycophenolate mofetil is second-line treatment in methotrexate-resistant severe and disabling disease.
- Severe, disabling, or rapidly progressive disease may be treated with monthly methylprednisolone intravenous pulse therapy in combination with weekly low-dose methotrexate.
- Therapies with ultraviolet A1 (not widely available in the United States) or systemic or bath psoralen plus ultraviolet A have been reported effective in small, prospective uncontrolled trials.

Pediatric Considerations

- Linear scleroderma is more common in children. Ultraviolet A1 is considered preferred therapy but is not widely available.
- Early intervention is important in children to decrease limb-length discrepancy and contractures. Aggressive treatment by a pediatric dermatologist will often involve oral steroids and methotrexate and referral to orthopedics.

Pearls

- Plaque and generalized morphea are not systemic sclerosis—the patient should be reassured that the condition is benign and the lesions typically soften in time.
- Half of patients will have lesion softening within the first 4 years.
- Raynaud's phenomenon and sclerodactyly are associated with systemic sclerosis, and not with plaque morphea.

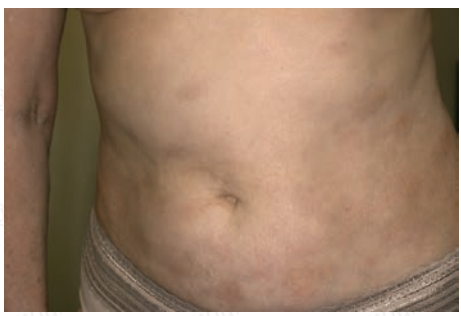

Fig. 14.33 Multiple depressed, ill-defined, firm plaques of morphea on the abdomen.

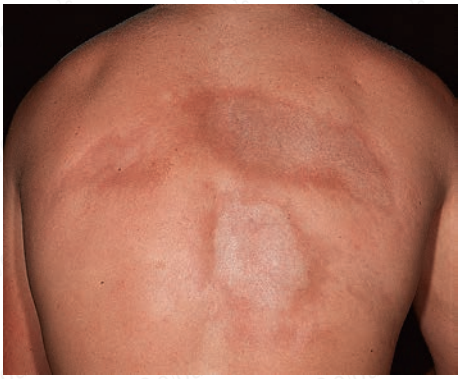

Fig. 14.34 Localized morphea. Early lesions with a violaceous or lilac-colored border, indicating active inflammation. The center of lesions is white-yellow and firm.

Fig. 14.35 Multiple ill-defined violaceous plaques of morphea on the breasts.

Fig. 14.36 Morphea. Frontoparietal linear morphea *(en coup de sabre)* is a depression suggestive of a stroke from a sword. Extensive lesions may cause hemifacial atrophy.

Light-Related Diseases and Disorders of Pigmentation 15

James G. H. Dinulos

Sun-Damaged Skin, Actinic-Damaged Skin, and Photoaging

Description

- Sun-damaged skin is easily recognizable and shows specific skin findings, resulting from damage due to ultraviolet radiation (UVR).

History

- Acute exposure to UVR results in sunburn and is especially caused by ultraviolet B (UVB) radiation.
- Chronic UVR exposure results in photoaging and skin cancer.
- Light-colored skin, genetic disorders (e.g., xeroderma pigmentosum), and certain medications (e.g., doxycycline and sulfa-based medications) predispose to sunburn and photoaging.

Skin Findings

- Sunburn results from acute UVR and produces pain, redness, and peeling.
- Immediate pigment darkening occurs minutes after ultraviolet A (UVA) radiation and fades in 6 to 8 hours.
- Delayed tanning occurs 48 to 72 hours after exposure to UVB and UVA radiation and is due to new pigment production.
- Chronic UVR exposure results in hyperpigmentation, hypopigmentation, telangiectasia, rhytides (e.g., fine lines and furrows), large sebaceous glands, comedones, milia, bruises, and atrophy of the skin.
- Certain cutaneous sites develop characteristic patterns, such as deep furrows on the back of the neck (cutis nuchae rhomboidalis) and red-brown discoloration on the sides of the neck (poikiloderma of Civatte)

Laboratory

- No testing if necessary to diagnose sun-damaged skin.

Differential Diagnosis

- Sunburn differential diagnosis: phototoxic medication reaction, toxin-mediated erythema, underlying genetic skin disorder (e.g., xeroderma pigmentosum)
- Chronic sun exposure differential diagnosis: rosacea, premature aging syndrome

Course and Prognosis

- With proper sun precautions, use of sunscreen, and sun-protective clothing, photoaging can be minimized.

Treatment

- Sunburns should be treated with cool compresses, soothing creams (e.g., aloe vera or soy-based creams), nonsteroidal anti-inflammatory medicine (e.g., ibuprofen), and oral hydration.
- Effects of chronic sun exposure, such as wrinkles, can be treated with topical "antiaging" creams containing retinol and alpha-hydroxy acids, heat-based therapies (e.g., radiofrequency, laser and ultrasound),

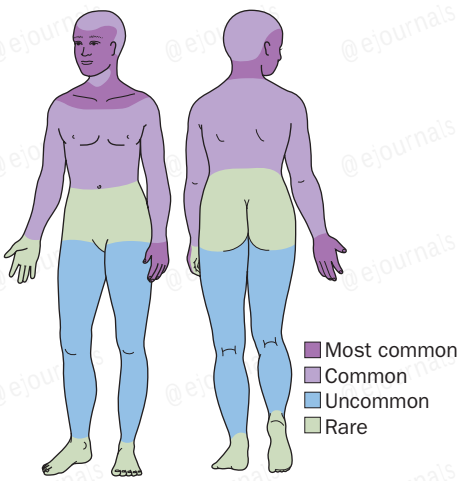

Fig. 15.1 Sun-damaged skin, actinic-damaged skin, photoaging distribution diagram.

Fig. 15.2 Cutaneous blood vessels are easily damaged by trivial external trauma to sun-damaged skin resulting in asymptomatic but unsightly ecchymosis. Aspirin therapy worsens solar purpura. Regular use of sunscreen and alpha-hydroxy acid moisturizer are of some benefit.

Fig. 15.3 Course wrinkling occurs after loss of elastic tissue and collagen. The skin surface is firm, smooth, and yellow.

Fig. 15.4 Solar elastosis is a sign highly characteristic of severe sun damage. There is coarsening and yellow discoloration of the skin.

Fig. 15.5 Sun-damaged skin. White, round, 2- to 3-mm papules (milia) and telangiectasia occur on the face in predisposed individuals with severely sun-damaged skin.

nonablative and ablative lasers, surgical face-lift, and lightening creams containing hydroquinone.

Pearls

- Sun-protective measures improve photoaging and prevent further damage.
- Patients seeking treatment for photodamage and cosmesis should commit to daily sunscreen use.

Fig. 15.6 Sun-damaged skin. Coarse, deep wrinkles radiate from the lateral margin of the eye. Degraded collagen cannot support hair follicles. The follicles expand, accumulate sebum, and form comedones.

Fig. 15.7 Sun-damaged skin. Bleeding occurs with the slightest trauma to the sun-damaged surfaces of the forearms and hands. The fragile skin tears easily and heals with crisscrossed scars.

Fig. 15.8 Sun-damaged skin. Sun-induced wrinkling on the back of the neck shows a series of crisscrossed lines. Reactive hyperplasia of melanocytes causes lentigines. Diffuse persistent erythema is prominent in fair-skinned people.

Fig. 15.9 Poikiloderma of Civatte. Chronic sun exposure may cause red-brown pigmentation with telangiectasia and atrophy on the sides of the neck in predisposed individuals. The *shaded area* under the chin is spared.

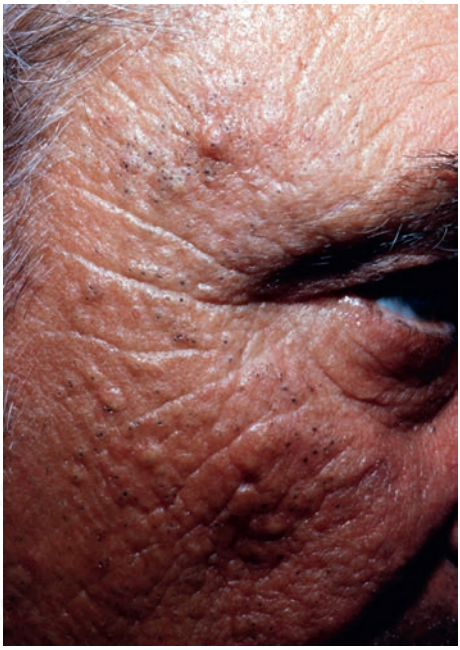

Fig. 15.10 Actinic comedones. Extensive sun exposure results in open and closed comedones.

Fig. 15.11 This photo-distributed rash is due to a quinolone antibiotic.

Fig. 15.12 Photodermatitis due to loratadine. Common over-the-counter medicines, such as loratadine, may cause photosensitivity.

Polymorphous Light Eruption

Description

- Polymorphous light eruption (PMLE) is an idiopathic, recurrent rash, occurring on sun-exposed sites, especially in the spring or with first sun exposure.

History

- PMLE is commonly referred to as sun poisoning or sun allergy.
- PMLE occurs in all races, at any age, but is most common in young women.
- Up to 10% of the population is affected, and it is considered the most common photodermatosis.
- Hereditary PMLE occurs in Inuit and people of Native American descent.
- Autosomal dominant inheritance with incomplete penetrance and variable expressivity has been described.
- Symptoms may include pruritus, malaise, chills, headache, and nausea.
- The rash tends to improve with increasing sun exposure ("hardening").
- The underlying pathogenesis is unknown, but it is thought to involve a delayed-type hypersensitivity reaction to an unknown antigen.

Skin Findings

- Pink pruritic papules, vesicles, and plaques appear minutes to days (up to 5 days) after sun exposure and fade over days to weeks.
- Initial symptoms are burning, itching, and erythema on exposed skin, such as the upper chest, back of the hands, extensor aspects of the forearms, and lower legs.
- PMLE tends to spare the face (except in hereditary form).

Laboratory

- Skin biopsy is helpful to rule out other photo-distributed rashes, such as lupus and porphyria.
- Serologic tests for lupus and porphyria should be ordered.

Differential Diagnosis

- Lupus erythematosus
- Photo-exacerbated rash (seborrheic dermatitis, rosacea)
- Phytophotodermatitis
- Erythropoietic protoporphyria

Course and Prognosis

- PMLE is persistent but may improve over the years.

Discussion

- UVA is the trigger in most cases, although the amount of exposure needed to trigger a flare varies.

Treatment

- Minimize sun exposure, especially between 10 AM and 2 PM.
- Sun-protective clothing should be encouraged.
- Apply broad-spectrum, UVA-blocking sunscreens, especially those containing avobenzone, titanium dioxide, and zinc oxide.
- Groups II to V topical steroids may relieve itch and fade the rash.

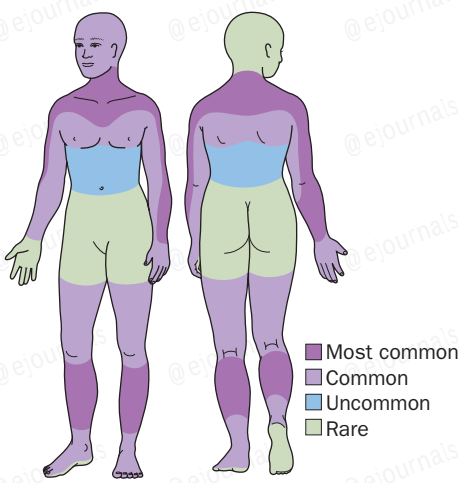

Fig. 15.13 Polymorphous light eruption distribution diagram.

- Oral steroids tapered over 2 weeks are useful in severe cases.
- Gradual increase in sunlight or UVR before intense sun exposure lessens the severity of PMLE.

Pearls

- Patients may be treated with UVB therapy in the spring to "harden" the skin before intense summer sunlight. UVB therapy is also effective to prevent PMLE before vacations in sunny climates.

Fig. 15.16 Polymorphous light eruption. Small papules are disseminated or densely aggregated on a patchy erythema.

Fig. 15.14 Polymorphous light eruption. The papular type is the most common form. Small papules are densely aggregated. The back of the hands is a common site. The rash itches and is sometimes painful. Lesions persist for 7 to 10 days.

Fig. 15.17 Polymorphous light eruption. The papulovesicular type occurs primarily on the arms, lower limbs, and the V area of the chest.

Fig. 15.15 Polymorphous light eruption. The papulovesicular type begins with urticarial plaques from which groups of vesicles arise.

Fig. 15.18 Polymorphous light eruption. Papules are localized and symmetrically distributed. They do not occur on the entire sun-exposed areas. Itching is not a constant feature.

Fig. 15.19 Polymorphous light eruption. Acute flare on the arms is coincident with the patient's first prolonged sun exposure of the spring.

Fig. 15.21 Polymorphous light eruption. Urticarial plaques on the legs with papules on the arms.

Fig. 15.20 Polymorphous light eruption. Discrete monomorphic pruritic papules limited to sun-exposed skin.

Fig. 15.22 Polymorphous light eruption. Patients who are highly sensitive to the sun may develop vesicles. A short course of low-dose prednisone may abate a severe reaction.

Porphyria Cutanea Tarda

Description

- Porphyria cutanea tarda (PCT) is a disorder of the porphyrin–heme biosynthetic pathway (decreased catalytic activity of uroporphyrinogen decarboxylase), resulting in photosensitivity and skin fragility.

History

- There are two types of PCT: acquired (more common), due to decreased enzyme function in the liver; and inherited (autosomal dominant), due to decreased enzyme function in all tissues.
- Precipitating factors include alcohol, estrogen, dialysis, iron, hepatitis C, and HIV.
- PCT patients have an increased risk for hepatocellular carcinoma.

Skin Findings

- Early changes include erythema, edema, and vesicles.
- Blisters occur in sun-exposed areas, such as the face and neck, dorsa of the hands, and forearms.
- Blisters rupture, leaving erosions and ulcers that heal with scarring.
- Milia form in previously blistered sites.
- Chronic changes include facial hypertrichosis and hyperpigmentation, particularly on the temples and on periorbital skin.
- Sclerotic changes and increased skin fragility occur on the cheeks, posterior neck, ears, and fingers ("scleroderma-like").

Nonskin Findings

- Liver disease occurs in association with ethanol abuse, estrogens, aromatic hydrocarbons, dialysis, sarcoidosis, and infection with hepatitis B and C.

Laboratory

- Porphyrin studies are done of the blood, urine, and stool.
- Because of high concentrations of porphyrin pigment, urine may appear red-brown ("port-wine urine").
- Urine in PCT patients will fluoresce pink to red under Wood's light examination.
- Consider a liver imaging study (computed tomographic scan or ultrasound) to evaluate for hepatocellular carcinoma.

Differential Diagnosis

- Pseudoporphyria (commonly from nonsteroidal anti-inflammatory drugs)

Course and Prognosis

- PCT in association with alcohol abuse tends to be chronic and relapsing.

Treatment

- Patients should eliminate triggers, such as alcohol and estrogens.
- For iron overload, phlebotomy is the treatment of choice.
- Hydroxychloroquine or chloroquine accelerates the excretion of porphyrins and may induce remission within 6 to 9 months.

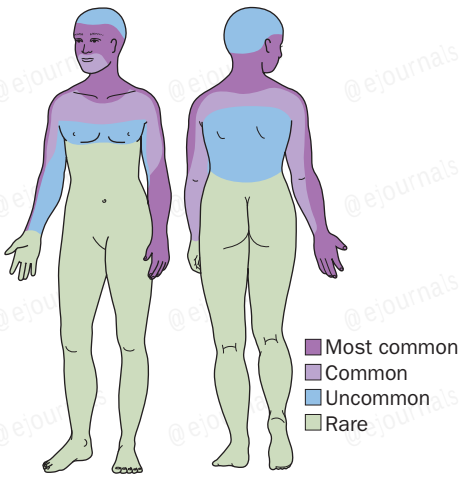

Fig. 15.23 Porphyria cutanea tarda distribution diagram.

Fig. 15.24 Porphyria cutanea tarda. Healing erosions and crusts are limited to the dorsal hands.

Fig. 15.25 Porphyria cutanea tarda. The clinical features in order of frequency are blistering in sun-exposed areas, facial hypertrichosis, hyperpigmentation, and sclerodermoid changes.

Fig. 15.26 Porphyria cutanea tarda. Blisters formed on a noninflamed base after sun exposure.

Fig. 15.27 Porphyria cutanea tarda. This classical presentation shows erosions, vesicles, and bullae localized to the backs of the hands.

Fig. 15.28 Porphyria cutanea tarda. White milia form during the healing process and are permanent.

Fig. 15.29 Pseudoporphyria. Bullae, hyperpigmentation, and scarring can occur with sun exposure in patients taking nonsteroidal anti-inflammatory drugs, such as naproxen.

Fig. 15.30 Variegate porphyria is a rare genetic condition caused by a deficiency of protoporphyrinogen oxidase, which is important in porphyrin–heme metabolism. The scaling and hyperpigmentation are due to photosensitivity.

Vitiligo

Description

- Vitiligo is an acquired disorder characterized by loss of functional melanocytes, resulting in depigmentation.

History

- One percent of the population is affected, and half of patients experience onset before age 20 years.
- Both genders are affected equally.
- There is a positive family history in 30% of affected patients.
- Vitiligo may begin after an inciting event, such acute illness, emotional stress, or trauma to the skin.

Skin Findings

- White macules coalesce into patches, and there may be pigmentation around hair follicles.
- There are two types of vitiligo (segmental and nonsegmental), although some patients exhibit both patterns.
- Segmental vitiligo does not cross the midline.
- Nonsegmental vitiligo may be widely distributed or localized to the acral sites (e.g., distal extremities, face, and gluteal region).

Nonskin Findings

- Vitiligo may be association with autoimmune diseases, such as thyroiditis, pernicious anemia, Addison's disease, systemic lupus erythematosus, rheumatoid arthritis, and diabetes.
- Vitiligo may be associated underlying genetic syndromes (e.g., Vogt–Koyanagi–Harada syndrome).

Laboratory

- Skin biopsy is usually not necessary.
- Laboratory evaluation for lupus, rheumatoid arthritis, thyroid disease, and a complete blood count may be helpful if supported by history and physical examination.

Differential Diagnosis

- Lupus erythematosus
- Pityriasis alba
- Piebaldism
- Tinea versicolor
- Leprosy

Course and Prognosis

- The course of vitiligo is highly variable—it may remain localized or rapidly result in generalized depigmentation.

Treatment

- Broad-spectrum sunscreen and sun-protective clothing are helpful.
- Concealing and camouflaging agents (Dermablend, Covermark, and Elizabeth Arden Concealing Cream) may be helpful for some patients.
- Topical treatments include corticosteroids (watch for skin thinning) and calcineurin inhibitors (tacrolimus and pimicrolimus).

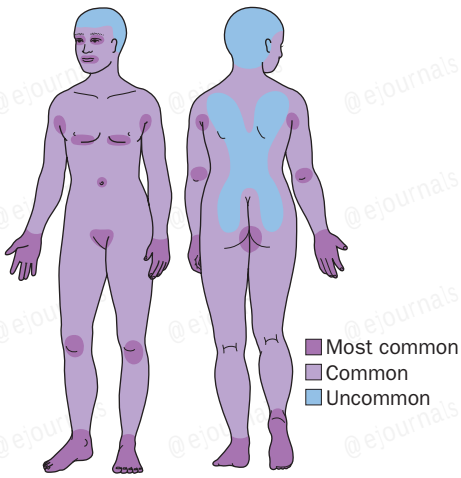

Fig. 15.31 Vitiligo distribution diagram.

Fig. 15.32 Vitiligo. Trichrome pigmentation with areas of pigment loss, normal pigmentation, and areas of intermediate pigmentation.

Fig. 15.33 Vitiligo. Typical pattern of depigmentation containing discrete islands of repigmentation from follicles.

Fig. 15.34 Vitiligo patch on the face. Depigmentation usually extends to involve local hairs.

- Phototherapy may include psoralen plus UVA, narrow-band UVB, and excimer laser (308 nm).
- Autologous skin transfer (e.g., minigrafting) may be used when medical and phototherapy fail.

Fig. 15.35 Vitiligo. Broad-spectrum sunscreen use should be encouraged to protect depigmented areas.

Fig. 15.36 Vitiligo. The margins of the lesions may become more hyperpigmented. The borders are sharply defined.

- Patients with involvement of more than 40% of the body surface may choose to remove the remaining normal pigment with 20% monobenzone (Benoquin cream).

Pearls

- Proper treatment requires a frank discussion of the patient's goals, reasonable expectations, and risks and benefits of treatment.
- Topical therapy, combined with phototherapy, is the most effective treatment, especially on the face.

Fig. 15.37 Vitiligo. Examine the axillae, groin, and anal area in all patients suspected of having vitiligo. These areas are commonly involved or may be the only areas involved.

Fig. 15.39 Vitiligo on the back of the hand. This area is resistant to all forms of treatment.

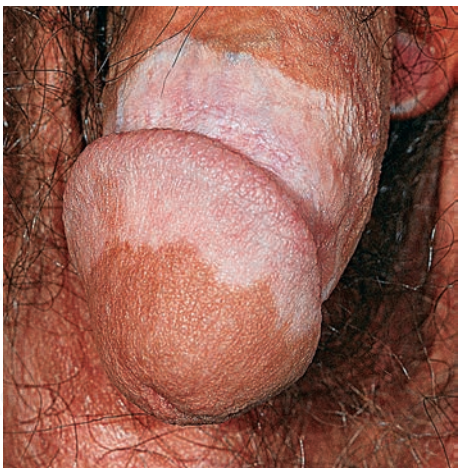

Fig. 15.38 Vitiligo. The genitals are frequently involved with vitiligo.

Fig. 15.40 Vitiligo. Treatment with either psoralen plus ultraviolet A (PUVA) or topical steroids stimulates repigmentation from perifollicular areas. These areas of repigmentation enlarge and merge to produce confluent repigmentation.

Fig. 15.41 Vitiligo. Loss of pigment may be partial or complete. Complex patterns are typical.

Fig. 15.42 Vitiligo. Several areas of depigmentation have merged to form large areas of pigment loss.

Idiopathic Guttate Hypomelanosis

Description

- Idiopathic guttate hypomelanosis is a common dermatosis, consisting of small white macules on sun-exposed surfaces of the upper and lower extremities.

History

- Idiopathic guttate hypomelanosis occurs in 50% to 70% of people older than 50 years.
- Women are more commonly affected and are often concerned about the appearance.
- Multiple family members are likely to be affected, suggesting an inherited component.

Skin Findings

- Multiple distinct white macules, often in the setting of sun-damaged skin, occur most commonly on the extremities.

Laboratory

- Skin biopsy is not necessary.
- Potassium hydroxide preparation will help evaluate for fungal infection.

Differential Diagnosis

- Vitiligo
- Tinea versicolor
- Chemically induced hypomelanosis from occupational exposure to depigmenting agents
- Tuberous sclerosis
- Pityriasis alba
- Seborrheic keratosis

Course and Prognosis

- The number of lesions increases with age.
- The lesions are stable in size and remain fixed.

Treatment

- Patients should be reassured and encouraged to take sun-protective measures.
- White macules can be camouflaged with tinted makeup, such as Covermark or Dermablend.
- Salon sunless spray tans provide good coverage when properly applied.

Pearls

- Reassure patients that idiopathic guttate hypomelanosis is not vitiligo.

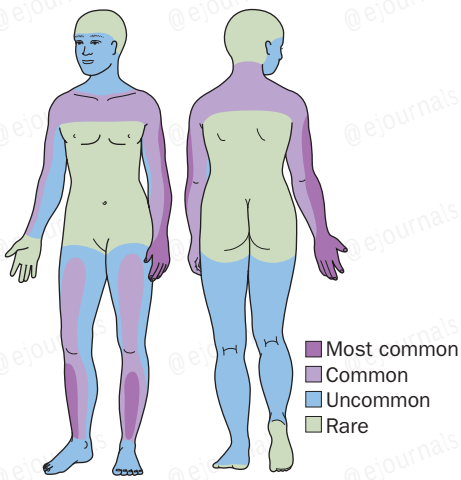

Fig. 15.43 Idiopathic guttate hypomelanosis distribution diagram.

Fig. 15.44 Idiopathic guttate hypomelanosis. Scattered white macules and lentigines are signs of sun damage on this woman's lower leg.

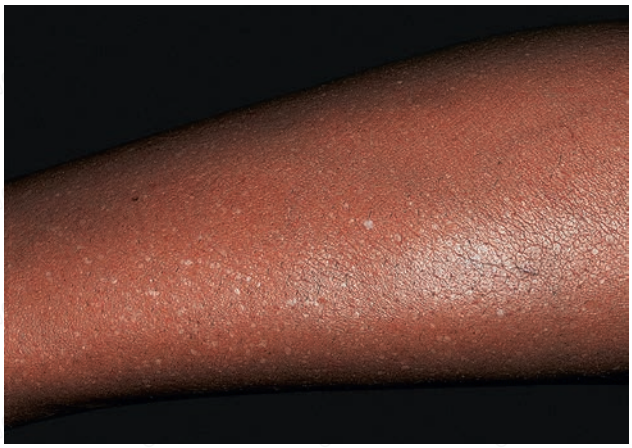

Fig. 15.45 Idiopathic guttate hypomelanosis is characterized by 2- to 5-mm white spots with sharply demarcated borders. They are a sign of photodamage.

Lentigo (Plural Lentigines), Juvenile Lentigo, Solar Lentigo

Description

- Common, benign, brown macules occurring on sun-exposed skin in whites and some Asians.

History

- Three lesion types are described: freckles (ephelides), juvenile lentigo, and solar lentigo.
- All three are similar in size, distribution, and clinical appearance.
- They differ in age of onset, clinical course, and relationship to sun exposure.

Freckles

- Freckles appear in childhood and occur as an autosomal dominant trait.
- They are usually confined to the face, arms, and upper trunk.
- They become more numerous and darken in response to sun exposure.
- Freckles lighten without UVR exposure and often completely fade in the winter.

Juvenile Lentigines

- Juvenile lentigines appear in childhood, with an average number of 30 per child.
- Juvenile lentigines do not increase in number, become larger, or darken in response to sunlight.
- Unlike freckles, juvenile lentigines do not fade in the absence of sunlight.
- Juvenile lentigines may be a part of certain hereditary syndromes.

Solar Lentigines

- Solar lentigines increase in number and size with advancing age.
- Roughly 75% of white people older than 60 years have one or more solar lentigines.
- Solar lentigines indicate sun damage due to UVR.

Skin Findings

- Freckles are uniformly colored macules (1–2 mm) with sharply defined borders.
- Freckles may be red, tan, and light brown.
- The degree of cutaneous involvement ranges from a few lesions to hundreds with near confluence.
- Juvenile lentigines are round to oval macules ranging in size from 2 to 10 mm.
- Juvenile lentigines are darker than freckles and are tan, brown, and black.
- Solar lentigines are 2- to 20-mm oval macules, seen on a background of sun-damaged skin.

Nonskin Findings

- Lentigines are a feature of rare autosomal dominant syndromes.
- Peutz–Jeghers syndrome consists of multiple lentigines of the oral mucosa with associated intestinal polyposis.
- The LEOPARD syndrome consists of multiple lentigines, electrocardiogram abnormalities, ocular disorders, pulmonary stenosis, abnormalities of genitalia, retardation of growth, and deafness.
- The LAMB or NAME syndrome consists of lentigines, atrial and/or mucocutaneous myxomas, myxoid neurofibromas, ephelides, and blue nevi.

Laboratory

- Skin biopsy may be helpful to exclude other pigmented lesions.

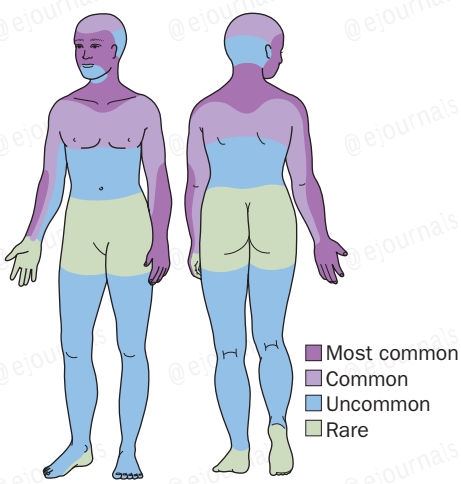

Fig. 15.46 Lentigines distribution diagram.

Fig. 15.47 Reactive hyperplasia of melanocytes causes persistent pigmentation in the form of solar lentigines on the neck and upper back. These permanent lesions may occur after one bad episode of sunburn.

Fig. 15.48 Lentigo. The lesions vary in size from 2 to 20 mm and become more numerous with advancing age. The lesion should be carefully examined. Seborrheic keratosis and melanoma have a similar appearance.

Fig. 15.49 Lentigo. Labial lentigines (labial melanotic macule) occur on the vermilion border of the lower lip. These brown macules have a smooth border and are benign.

Fig. 15.50 Solar lentigo (liver spots) appears on the face, arms, dorsa of the hands, and upper trunk after a single episode of sunburn or after years of sun exposure. These flat brown macules increase in number and size.

Fig. 15.51 Solar lentigo (liver spots) occurs in sun-exposed areas of the face, arms, and hands.

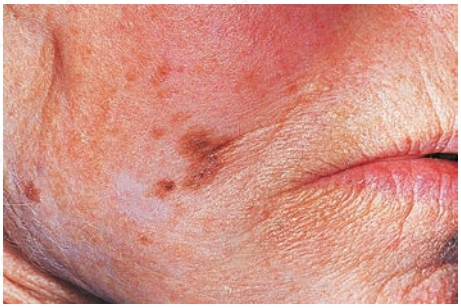

Fig. 15.52 Lentigo. A biopsy should be taken from any lentigo that develops a highly irregular border, or where there is a localized increase in pigmentation, or localized thickening, to rule out lentigo maligna melanoma.

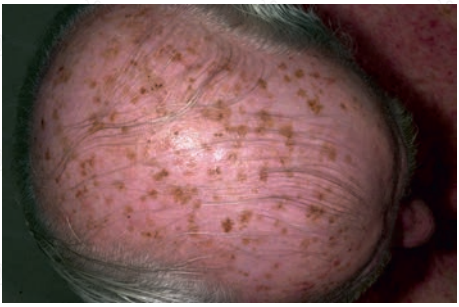

Fig. 15.54 Lentigo. Lentigines accumulate over years on the scalp of men with male-pattern baldness. Such men should be encouraged to wear a hat for sun protection.

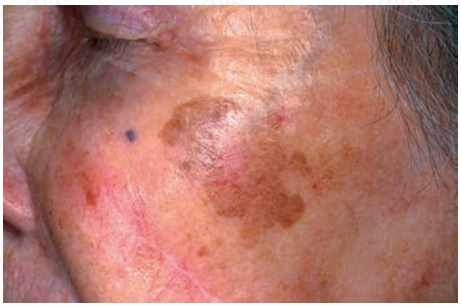

Fig. 15.53 Lentigo. Dermatoscopic and skin biopsy should be considered for this large, irregularly pigmented macule.

Fig. 15.55 Lentigo. Confluent lentigines on the dorsal hands of an older patient.

Differential Diagnosis

- Flat seborrheic keratoses
- Spreading pigmented actinic keratosis
- Lentigo maligna
- Junctional nevus
- When numerous lentigines are present, consider the possibility of an associated syndrome, such as Peutz–Jeghers, LEOPARD, or NAME (LAMB)

Course and Prognosis

- Freckles appear in early summer and usually fade by early winter.
- Juvenile and solar lentigines persist year-round.

Treatment

- Freckles do not require treatment and will fade in the winter months.
- Sunscreens prevent the appearance of new freckles and darkening of existing freckles.
- Juvenile lentigines and solar lentigines are benign and do not require treatment.
- Monitor existing lesions for interval change. Stable lesions do not require treatment, although it may be requested for cosmetic reasons.
- Hydroquinone solutions, tretinoin, azelaic acid cream, and glycolic acid peels and creams reduce pigmentation over weeks to months.
- Light cryosurgery is also effective but may result in depigmentation.

Pearls

- Changing lentigines should undergo biopsy to rule out melanoma.
- Labial lentigines (labial melanotic macule) occur on the vermilion border of the lower lip. These brown macules have a smooth border and are benign.

Fig. 15.56 Fair-skinned individuals develop lentigines as a delayed response to sunburn.

Fig. 15.57 Lentigo. Sharply defined melanotic macule on the lower lip. Such lesions are benign and persistent and are constant in appearance over years.

Melasma (Chloasma, Mask of Pregnancy)

Description

- Melasma is acquired brown hyperpigmentation of the face and neck in genetically predisposed women.

History

- Melasma is more common in women with darker skin tones.
- Pigmentation develops slowly and is more prevalent after sun exposure.
- Melasma commonly occurs during the second or third trimester of pregnancy and in some women taking oral contraceptives.

Skin Findings

- Symmetric brown patches, occurring on the forehead, cheek, upper lip, and chin.

Differential Diagnosis

- Postinflammatory hyperpigmentation
- Lentigines

Course and Prognosis

- Usually after pregnancy or with discontinuation of contraceptives, the pigment fades slowly over months.

Treatment

- Minimize sun exposure at midday and wear a hat.
- Use sunscreens that block both UVA and UVB.
- Physical sun blockers containing zinc or titanium are most effective.
- Depigmentation may be done with bleaching creams that contain hydroquinone.
- Hydroquinone can be an irritant and a sensitizer.
- Compounded products containing higher concentrations of hydroquinone may produce cutaneous ochronosis.
- Tretinoin cream 0.025%, 0.05%, 0.1% (Retin-A) and tretinoin emollient cream 0.05% (Renova) enhance the effectiveness of hydroquinones.
- Tretinoin is also effective as a solo agent.
- Combination products containing tretinoin, hydroquinone, and fluocinolone (Tri-Luma) may be more effective and more convenient. This is applied once each day for a maximum duration of 6 months.
- Azelaic acid (Finacea cream) with or without tretinoin is safe during pregnancy.
- Kojic acid is available in compounded and salon products as a bleaching agent.
- Superficial peels with glycolic acid hasten the effects of tretinoin and hydroquinone.

Pearls

- Sun avoidance is mandatory to prevent and lighten melasma.
- Patients must be made aware that treatment requires several weeks and strict sun protection.

Fig. 15.58 Melasma. The pigmentation develops slowly without signs of inflammation and may be faint or dark.

Fig. 15.59 Melasma. The forehead, malar eminences, upper lip, and chin are most frequently affected.

Fig. 15.60 Severe melasma on the forehead, midcheek, and upper lip in this patient with type IV skin. This patient would benefit from Tri-Luma cream and a broad-spectrum sunblock with an SPF of 30 or higher.

Benign Skin Tumors 16

M. Shane Chapman

Seborrheic Keratosis

Description

- A seborrheic keratosis is a common, benign, persistent epidermal lesion with variable clinical appearance.
- It is one of the most common benign growths seen on the skin.
- These keratoses have multiple clinical variations and can be easily be confused with other cutaneous malignancies.

History

- Seborrheic keratoses are unusual before 30 years of age.
- Most people develop at least one seborrheic keratosis in their lifetime.
- Males and females are equally affected.
- Lesions may be localized to the areola in both males and females.
- The tendency toward multiple seborrheic keratoses may be inherited.
- Keratoses are usually asymptomatic, but sometimes they are cosmetically bothersome.
- Depending on the location, the lesion can be subject to irritation, trauma, and bleeding.

Skin Findings

- There are usually multiple lesions, which can arise at any site except the lips, palms, and soles.
- The size and surface appearance of the lesions vary considerably.
- Most seborrheic keratoses are between 0.2 and 2 cm in diameter, although larger lesions can occur.
- Lesions may be flat or raised, and the surface may be smooth, velvety, or verrucous.
- Retained keratin cysts may be seen just under the surface.
- The color of lesions is extremely variable, including white, pink, brown, and black, and the color may vary within a single lesion.
- Lesions tend to be sharply demarcated and round to oval in shape but can be asymmetric.
- Thin seborrheic keratoses have a characteristic "stuck-on" appearance and waxy texture.
- Thicker keratoses have an elevated surface that tends to crumble when rubbed or picked.
- Dermatosis papulosa nigra describes the darkly pigmented seborrheic keratoses of the face seen more commonly in African Americans.
- Dermatosis papulosa nigra lesions are 1- to 2-mm, dark-brown keratotic papules concentrated around the eyes and upper cheeks, with an incidence of 30% to 35% in African American people.
- Stucco keratoses describe the small, white, firm seborrheic keratoses more commonly found on the lower legs and ankles of older white people.
- Inflamed seborrheic keratosis is a clinical description for a seborrheic keratosis with clinically obvious inflammation; there may be edema, erythema, and hemorrhage.

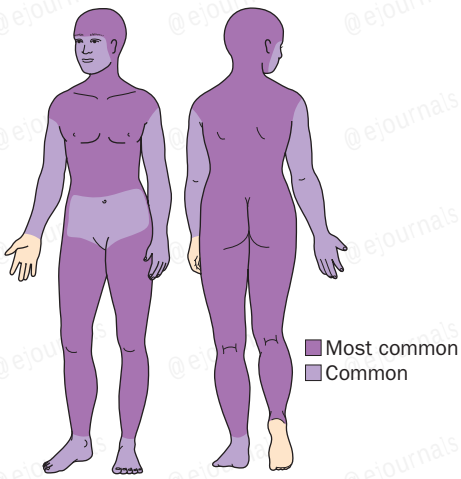

Fig. 16.1 Seborrheic keratoses distribution diagram.

Nonskin Findings

- The sign of Leser–Trélat is the sudden explosive onset of numerous seborrheic keratoses in association with internal malignancy.

Laboratory and Testing

- Several histologic subtypes of seborrheic keratosis are recognized.
- Acanthosis, hyperkeratosis, and papillomatosis are universal features.
- The degree to which these features develop varies considerably within individual lesions and among subtypes.
- Horn cysts and pseudohorn cysts are usually present.
- The degree of melanin pigment varies from almost none (stucco keratosis) to extreme (melanoacanthoma).
- Inflamed seborrheic keratoses show marked dermal inflammation, sometimes making the diagnosis difficult.

Course and Prognosis

- Unless disturbed, seborrheic keratoses tend to persist and grow slowly and become elevated with time.
- Some lesions may be removed by trauma, especially if located in the flexural skinfold areas.

Discussion

- Raised or pedunculated seborrheic keratoses may be indistinguishable from skin tags and compound melanocytic nevi.
- Flat seborrheic keratoses may mimic spreading pigmented actinic keratosis or superficial spreading melanoma. If doubt exists, a skin biopsy should be performed.
- Although seborrheic keratoses have no malignant potential, there are rare reports of melanoma, basal cell carcinoma, and squamous cell carcinoma developing within a seborrheic keratosis.
- A biopsy should be performed for a significantly changing seborrheic keratosis, looking for a malignancy.

Treatment

- Treatment may be indicated for symptomatic lesions.
- Lesions in areas of friction and frequent trauma often become irritated and symptomatic.
- Removal is often requested for discomfort or for cosmetic reasons.
- Patients should be informed that cosmetic removal of seborrheic keratoses is not usually covered by medical insurance.
- Cryosurgery is effective for flat or minimally raised lesions.
- Thicker lesions are best removed by cautery and curettage under local anesthesia.
- Residual scarring, if any, is minimal. Applying gentle pressure to the surrounding skin often provides enough tension to allow for easy curettage of lesions.
- Hypopigmentation and hyperpigmentation are possible side effects of cryotherapy or any method of removal.

Pearls

- Seborrheic keratoses are common benign growths with multiple variants that can mimic other, more worrisome skin tumors.
- Removal is not necessary unless lesions become inflamed and symptomatic.
- Some keratoses are heavily pigmented, resembling melanoma, and therefore may need histologic confirmation.
- When dermatologists unknowingly remove melanomas, it is thought that they are seborrheic keratoses clinically in 85% of cases.

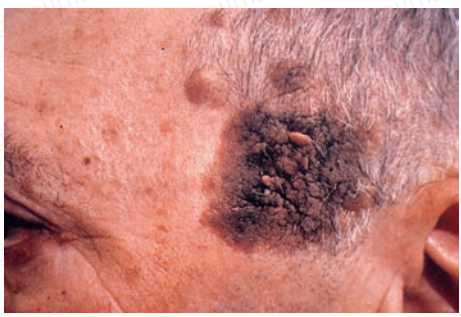

Fig. 16.2 Seborrheic keratoses. Large, pigmented, waxy verrucous patch characteristic of a seborrheic keratosis.

Fig. 16.3 Seborrheic keratoses. Large, waxy, light and dark brown seborrheic keratoses, covering the back. The asymmetry and color variation can be worrisome for melanoma, but the generalized nature of these lesions is characteristic of seborrheic keratoses.

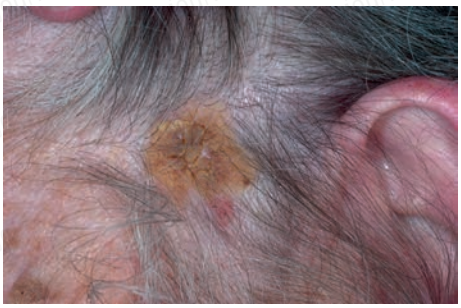

Fig. 16.4 Seborrheic keratoses. A 1-cm yellow-brown fissured patch on the scalp. Seborrheic keratoses in this area can be frequently traumatized and symptomatic.

Fig. 16.5 Seborrheic keratoses. Multiple seborrheic keratoses surrounding the areola. Keratoses in this location can be disconcerting to patients, but these are benign.

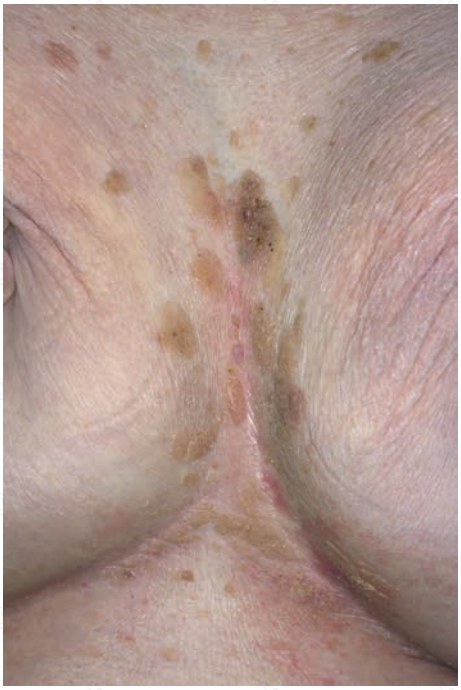

Fig. 16.6 Seborrheic keratoses. Diffuse small and large seborrheic keratoses between the breasts folds, another region where multiple keratoses can occur and become frequently inflamed and irritated.

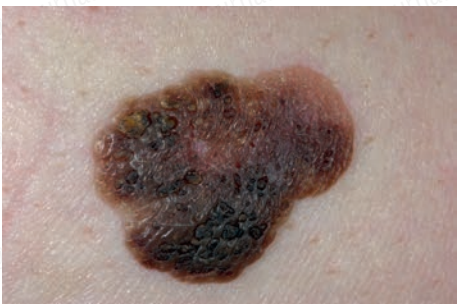

Fig. 16.7 Seborrheic keratoses. A large, asymmetric, smooth waxy plaque with multiple keratin-filled horn cysts within the lesion.

Melanoma Mimics

Fig. 16.8 Melanoma mimics. Some seborrheic keratoses may have many of the features of superficial spreading and nodular melanoma. The colors are variable, and the white areas look like areas of tumor regression. A magnified view shows several horn cysts that are typically found in seborrheic keratoses and rarely present in melanoma. A biopsy should always be performed if melanoma is suspected.

Seborrheic Keratosis
Rough Surface Lesions

Fig. 16.9 Rough-surfaced lesions. The rough-surfaced seborrheic keratoses are the most common benign skin tumor. They are oval to round, flattened domes with a granular or irregular surface that crumbles when picked. Flatter lesions are found on the arms and legs. Patients often refer to these lesions as warts because of the similar appearance.

Seborrheic Keratosis
Smooth Surface Lesions

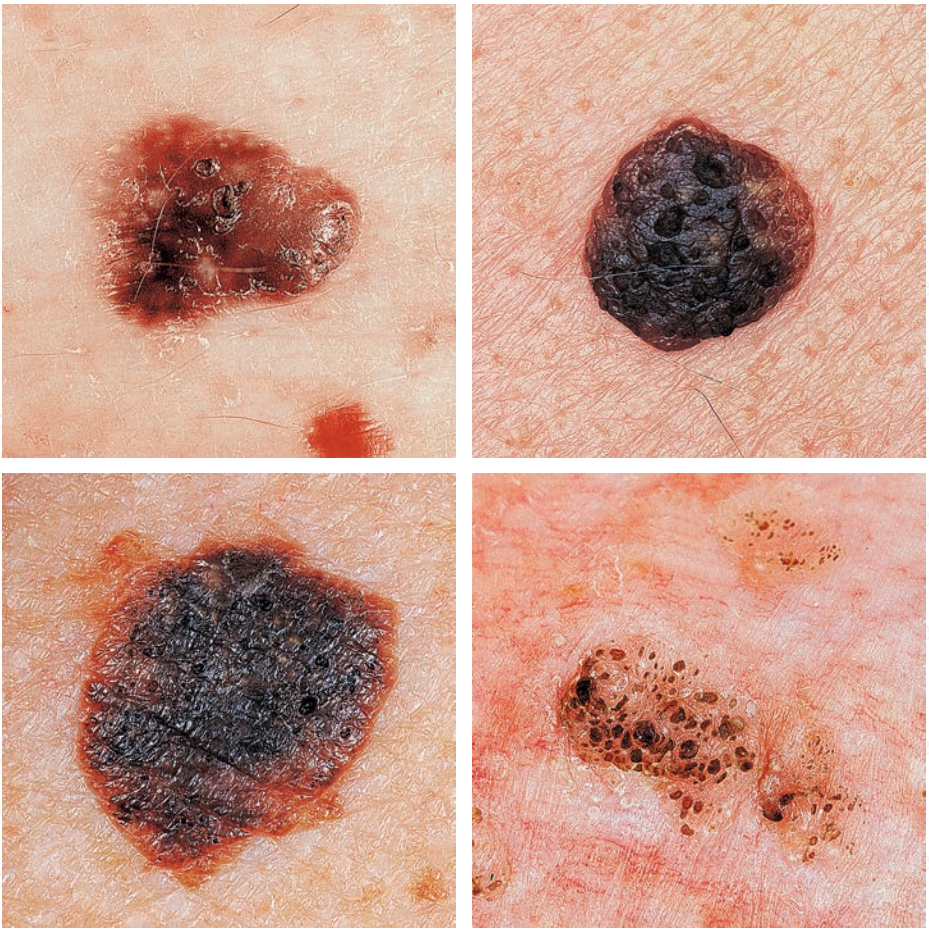

Fig. 16.10 Smooth-surfaced, dome-shaped tumors have white or black pearls of keratin, 1 mm in diameter, embedded in the surface. These horn pearls are easily seen with a hand lens. Melanomas do not contain horn pearls.

Seborrheic Keratosis
Irritated

Fig. 16.11 Irritated seborrheic keratoses become slightly swollen and develop an irregular, red flare in the surrounding skin. They may develop into a bright-red, oozing mass with a friable surface that resembles an advanced melanoma or a pyogenic granuloma.

Fig. 16.12 Irritated seborrheic keratosis. Lesions can become very large and disfiguring and resemble melanoma. Examine the surface closely with a hand lens. Look for horn pearls that are only found in seborrheic keratoses.

Fig. 16.13 Irritated seborrheic keratosis. Numerous lesions may appear on the face in predisposed people.

Fig. 16.14 Irritated seborrheic keratosis. Lesions are often concentrated in the presternal area and under the breasts. Chafing from clothing or from maceration in this intertriginous area can start irritation.

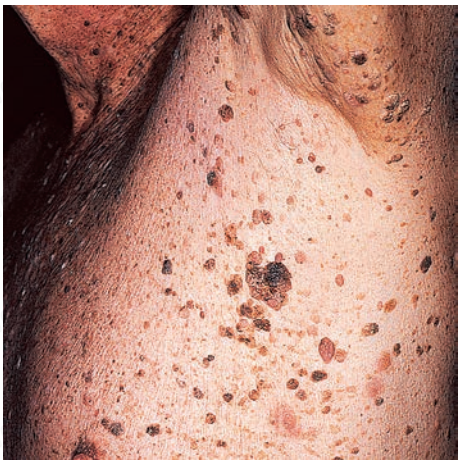

Fig. 16.15 Irritated seborrheic keratosis. The number varies from less than 20 in most people to numerous lesions on the face or trunk.

Fig. 16.16 Irritated seborrheic keratosis. Lesions may be localized to the areola in both men and women.

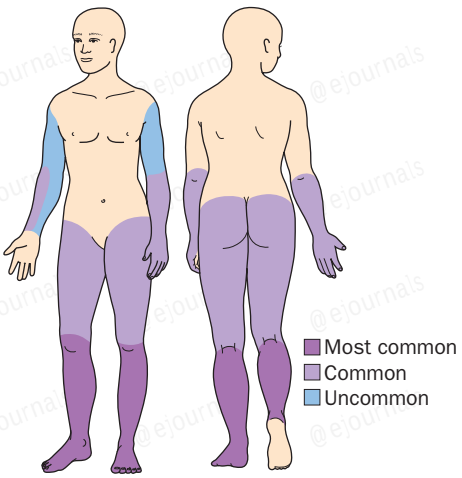

Fig. 16.17 Stucco keratoses are white, papular, warty lesions occurring on the lower legs, especially around the Achilles tendon area, and the dorsum of the foot. The 1- to 10-mm lesions are round, very dry, and stuck-on, considered by most patients to be simply manifestations of dry skin. The dry surface scale is easily picked intact from the skin without bleeding, but it recurs shortly thereafter. Cryosurgery in this area may produce excessive hyperpigmentation. Curettage of individual lesions may be the best treatment option for those few patients who request their removal.

Skin Tags

Description

- Skin tags are common benign fleshy papules occurring in the skinfolds.

History

- Skin tags, or acrochordons, are uncommon before 30 years of age but are common thereafter.
- Women are affected more often than men.
- Roughly 25% of adults have at least one skin tag.
- Most patients with skin tags have only a few lesions.
- They are more common in overweight persons.
- There may be a familial tendency toward multiple skin tags.
- Undisturbed lesions are usually asymptomatic.
- As a result of their location, skin tags may become irritated by friction, jewelry, or clothing.
- They may become tender when traumatized, twisted, torn, or thrombosed.

Skin Findings

- A skin tag is a skin-colored or brown 1- to 5-mm papule.
- Papules may be flat or filiform, although most are soft, fleshy, and pedunculated on a thin stalk.
- The axillae are the most common location, followed by the neck.
- Lesions also occur on the eyelids as well as in other intertriginous areas, such as the inframammary and inguinal creases.

Nonskin Findings

- A previously reported association between skin tags and colonic polyps has not been confirmed by further studies.
- Skin tags are part of Birt–Hogg–Dubé syndrome, which also includes trichodiscomas and fibrofolliculomas of the face, neck, and chest. Patients with this syndrome may have associated renal cell carcinoma, colonic adenomas, pulmonary cysts, and medullary carcinoma of the thyroid gland.

Laboratory

- Skin biopsy confirms a papule with a characteristic thinned epidermis and a loosely arranged fibrous stroma with capillaries.

Course and Prognosis

- Left undisturbed, skin tags persist indefinitely or fall off unknowingly.
- With torsion, skin tags may become thrombosed and tender.
- With this acute change, patients usually seek care because they are concerned about skin malignancy.
- Thrombosed skin tags often appear black, hemorrhagic, or both.
- Any delay in seeking care allows the residual skin tag time to fall off on its own; thus no residual lesion is seen.

Differential Diagnosis

- Warts
- Nevi
- Seborrheic keratosis

Treatment

- Asymptomatic skin tags do not require treatment.
- Patients often request removal because of tenderness or for cosmetic reasons.
- Patients should be informed that medically unnecessary removal of skin tags is usually not covered by medical insurance.

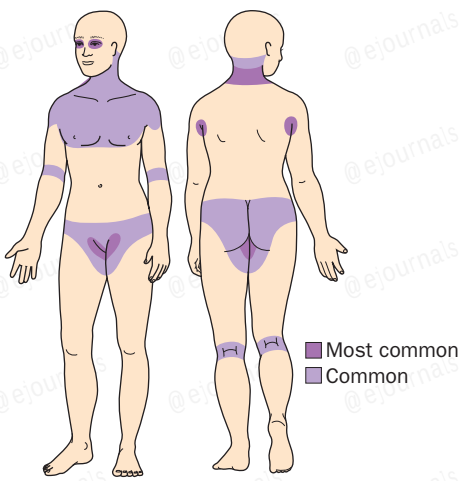

Fig. 16.18 Skin tags distribution diagram.

Fig. 16.19 Skin tags. Mostly commonly present as a soft papule on a thin stalk, variable colors, from flesh to pink, or lightly pigmented.

Fig. 16.20 Skin tags begin as tiny, brown or skin-colored, oval excrescences attached by a short, broad-to-narrow stalk.

- Skin tags are best treated by scissors excision with or without local anesthesia.
- Electrocautery and cryosurgery can also be used.
- The need to submit all skin tags for histologic review has been a topic of debate in recent years.
- Many dermatologists feel that histologic confirmation is usually not necessary.

Pearls

- Skin tags do not normally present a diagnostic dilemma.
- They can be inflamed, thrombosed, or tender and require treatment.
- Skin tags around the eyelids may resemble other skin tumors and may need a biopsy for confirmation.

Fig. 16.22 Skin tags occur around the eyes and may resemble warts.

Fig. 16.21 Skin tags are commonly found in the skinfolds or where chronic friction and rubbing occur. They can become numerous, large, and inflamed.

Dermatofibroma

Description

- Dermatofibroma is a common, benign, indolent, dermal papule most commonly occurring on the legs of adults.
- It can be pigmented and confused with melanoma.

History

- Dermatofibromas arise spontaneously in adults and occasionally in children.
- The etiology is unknown.
- The lesions occur more often in women.
- Lesions on the legs of women are subject to repeated trauma from shaving and can be annoying.
- Most are asymptomatic, but pruritus and tenderness may occur.
- Controversy exists as to whether the lesion represents a spontaneous benign neoplastic process or reactive hyperplasia in response to injury, but most patients do not recall a specific trauma to the area.
- Some patients note itching when the lesion is first noted and attribute this to an insect bite.
- Dermatofibromas tend to persist indefinitely while remaining stable in size and appearance.

Skin Findings

- Discrete, firm, pink dermal papules 3 to 5 mm in diameter are typical, but occasionally they can be larger than 3 cm.
- Most dermatofibromas are dome shaped, although some are depressed below the surrounding skin surface.
- The lesion is fixed within the skin but is movable over the underlying subcutaneous fat.
- On palpation, the lesion feels like a firm button and puckers and retracts below the surface with palpation.
- Dermatofibromas are typically flesh-colored to pink with a poorly defined rim of tan to brown pigmentation.
- Rarely, lesions may be blue to black as a result of hemosiderin deposition and resemble melanoma.
- The surface may be smooth and shiny to scaly or excoriated.
- Although dermatofibromas may arise on any cutaneous surface, most are found randomly distributed on the extremities.
- Lesions can be solitary or multiple.

Laboratory

- Skin biopsy shows a focal unencapsulated proliferation of spindle-shaped cells resembling fibroblasts, histiocytes, and collagen.

Course and Prognosis

- Dermatofibromas attain their maximum size over months to years and then persist indefinitely.
- Depending on location, lesions may be subject to repeated trauma from shaving or friction from clothing and footwear.

Discussion

- Lesions with large amounts of hemosiderin deep within the tumor may be blue to black and suggestive of nodular melanoma or pigmented dermatofibrosarcoma protuberans. Biopsy is warranted in such cases.
- Dermatofibroma can clinically mimic melanoma with a central pink nodule and surrounding pigmentation.
- Dermatofibrosarcoma protuberans resembles dermatofibroma histologically and, less commonly, clinically.

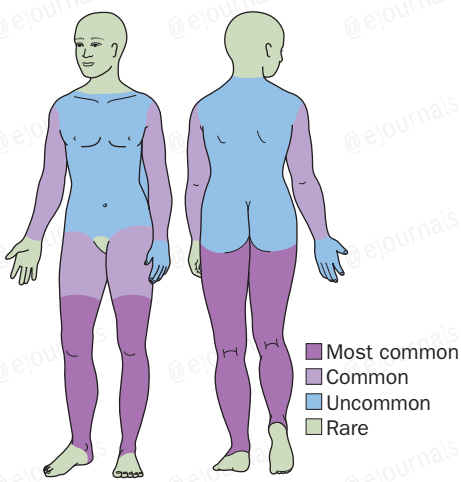

Fig. 16.23 Dermatofibroma distribution diagram.

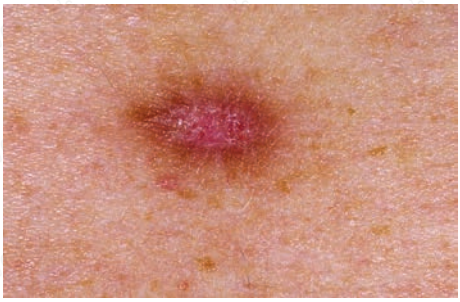

Fig. 16.24 A firm, indurated pink papule that puckers with palpation, characteristic of a dermatofibroma. Dermatofibromas frequently display a rim of light hyperpigmentation.

Fig. 16.26 This dermatofibroma is pink, smooth, and dome-shaped, with significant elevation above the skin surface, but has a characteristic firm, indurated feel with palpation.

Fig. 16.25 Dermatofibromas have various clinical presentations. This lesion is smooth and pink with scar-like elevation in the middle and a narrow rim of hyperpigmentation.

Fig. 16.27 Dermatofibroma. Early lesions can be elevated, firm, and pink and can be confused with skin cancer.

- This insidious malignancy usually occurs on the trunk and presents as a slow-growing, often recurrent, poorly defined red-purple nodule or plaque.
- Overall, the histologic findings are similar to those of dermatofibroma, so a superficial biopsy may be falsely reassuring.
- Deep punch or excisional biopsy that includes subcutaneous fat confirms that dermatofibrosarcoma protuberans is more cellular than most dermatofibromas.
- Malignant cells extend into the subcutaneous fat.

Treatment

- Dermatofibromas are benign skin tumors that do not require treatment unless they are symptomatic, repeatedly traumatized, or cosmetically bothersome. The patient should be assured that the lesion is benign.
- Surgical excision with primary closure is the treatment of choice for symptomatic lesions.
- Caution should be used when removing lesions for cosmetic reasons because the final appearance of the surgical scar may be less cosmetically acceptable than the original lesion.
- If the lesion is incompletely excised by shave excision, the patient should be warned of possible recurrence.
- Intralesional corticosteroid injection has been used to flatten elevated lesions. This form of treatment produces unpredictable results and is generally not recommended.

Pearls

- Dermatofibromas should be stable in size, appearance, and color. If they are not, they should be biopsied.
- Pigmented lesions that are suspected to be traumatized should be biopsied.
- A shave biopsy is not appropriate when the diagnosis is in question.
- An excision is optimal so that the entire lesion, including the deep dermal component, can be evaluated histologically.

Fig. 16.28 Dermatofibroma. New lesions are pink and elevated. After months the border becomes tan to brown, and the center retains the pink color.

Fig. 16.29 Dermatofibroma. The density of the brown pigmentation increases with time, and the distinction between the border and the pink becomes more apparent. Patients become concerned about melanoma with the increasing density of the pigmentation.

Fig. 16.30 Dermatofibromas retract beneath the skin surface during attempts to compress and elevate them.

Keloids and Hypertrophic Scars

Description

- A keloid is an exuberant scar that extends beyond the area of trauma, injury, or surgical scar.
- A hypertrophic scar is an exaggerated healing response to trauma, injury, or surgical scar.

History

- Males and females are affected with equal frequency.
- Keloids can occur at any age but tend to occur before age 30 years.
- Keloids are more common in darker skinned patients than white people.
- Hypertrophic scars and keloids can arise at any skin site.
- Most occur on the chest or head and neck area, including the earlobe.
- Lesions occur at sites of trauma and injury, which includes surgery, burns, piercing, acne, and sites of inflammation.

Skin Findings

- Normal scars are usually red and firm during the initial weeks to months of healing.
- Itching and tenderness are common for normal scars, hypertrophic scars, and keloids.

Hypertrophic Scars

- Hypertrophic scars have a similar color and texture compared with normal scars but are present for a longer period of time, lasting for months.
- They are larger and more raised than expected of scars from the injury.
- The surface is smooth, dome-shaped, and shiny with prominent vessels.
- One portion of a scar may appear normal, and another portion may appear to be hypertrophied.
- Unlike keloid scars, hypertrophic scars remain confined to the site of injury.

Keloids

- By definition keloids extend beyond the area of trauma or injury.
- Keloids are firm, red to violaceous, large, tender nodules.
- Keloids are usually hyperpigmented in darker skinned patients and red to purple in white skin.
- Some keloids are enormous and continue to expand over time, measuring 10 to 20 cm or more.
- Depending on the type of original injury, the lesion may be linear or nodular.
- In rare instances, keloids may arise spontaneously, without preceding trauma.
- Spontaneous keloids usually occur on the chest and shoulders.

Laboratory

- A skin biopsy is usually not needed to make the diagnosis.
- Biopsy can induce further scarring and should be used only if necessary.
- Hypertrophic scars contain randomly dispersed fibroblasts and whorled bundles of new collagen.
- Keloids extend beyond the wound margins and contain thick bands of eosinophilic collagen with fewer fibroblasts.

Course and Prognosis

- Hypertrophic scars tend to regress even without treatment, although it may take several years to reach a final outcome.

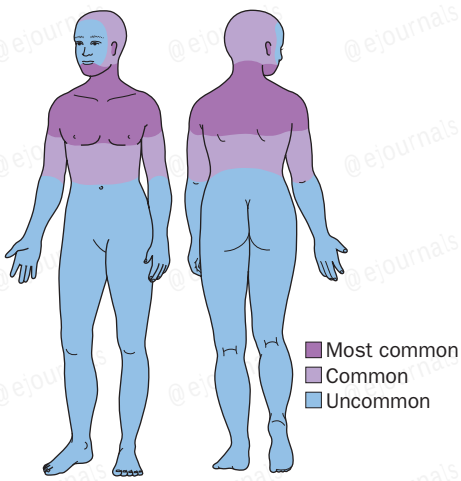

Fig. 16.31 Keloids and hypertrophic scars distribution diagram.

Fig. 16.32 A hypertrophic scar at a surgical site of "injury" that is tender, elevated, and pronounced.

Fig. 16.33 Keloids and hypertrophic scars. Large and small, multiple hypertrophic scars and keloids form in predisposed people after cystic acne.

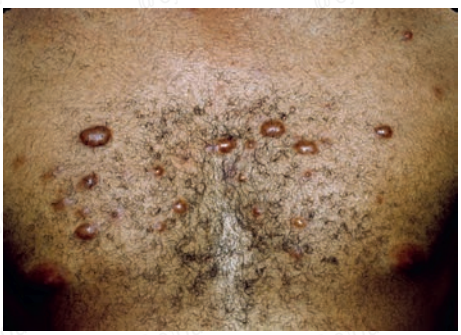

Fig. 16.34 Keloid nodules can occur on the midchest, either spontaneously or in association with acne inflammation, and are typically smooth, flesh-colored nodules that can be tender or asymptomatic.

- Keloid scars show no tendency toward regression and tend to slowly enlarge over time.

Differential Diagnosis

- Dermatofibrosarcoma protuberans
- Sarcoidosis (especially for facial keloids)

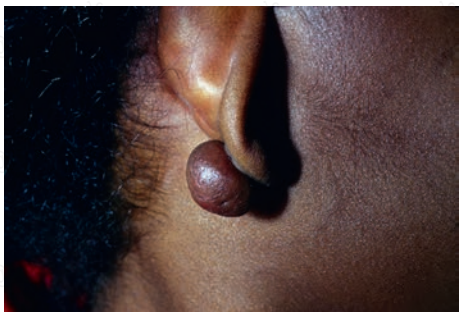

Fig. 16.35 Keloids occur after trauma, especially after ear-piercing, and appear as firm, tender, flesh-colored nodules that may extend from the front of the earlobe to the posterior earlobe and continue to enlarge indefinitely.

- Recurrence of original tumor, such as those arising in surgical scars from excision of malignancy

Discussion

- The diagnosis of a keloid and hypertrophic scar is usually straightforward.
- There is a history of localized trauma, and the injury site is intact.
- There is no history of prior injury in dermatofibrosarcoma protuberans.
- If doubt exists, biopsy can be performed to confirm.

Treatment

- People with a history of hypertrophic or keloid scars should be discouraged from having cosmetic procedures or body piercing.
- Both types of scar are best explained as unpredictable scarring.
- Patients who require surgical procedures in areas at increased risk for abnormal scarring should be advised of this possibility in advance and should be reminded at the time of suture removal.
- Despite meticulous surgical and postsurgical care, keloid and hypertrophic scars can still occur.
- This process is most likely determined genetically.
- The parents of a child who has had a procedure that resulted in a keloid or hypertrophic scarring need reassurance and a management plan.

- Early abnormal scarring typically responds better than older, less active scarring; early intervention is advised.
- Intralesional corticosteroid injection is the treatment of choice.
- Triamcinolone injected intralesionally at concentrations of 5 to 20 mg/mL is given at intervals of 2 to 4 weeks.
- Close follow-up is needed at higher concentrations to minimize the risk for overtreatment and permanent atrophy.
- Radiation therapy and more recently pulse dye laser therapy have been used for hypertrophic scars and keloids.
- Compression therapy and Silastic sheeting can be helpful but inconvenient.
- Topical silicon-containing gels have been marketed for the treatment of hypertrophic scars, although efficacy in all patients is questionable.
- Surgical correction of hypertrophic scars and keloids requires experience and careful monitoring.
- Keloid and hypertrophic scars tend to recur, sometimes larger, after surgical removal.
- A referral to a dermatologist or plastic surgeon with an interest in scar removal should be considered.

Pearls

- Hypertrophic scars and keloids are difficult to eradicate no matter which procedure is used.
- A patient with a family history or personal history should avoid unnecessary surgical procedures and body piercing.

Fig. 16.36 A keloid scar extends beyond the area of trauma. In this case a keloid formed after an excisional surgical procedure and continued to expand beyond the suture line.

Fig. 16.38 Very large keloids may form in the earlobe after ears are pierced. Darker skinned people are more predisposed to this.

Fig. 16.37 A keloid formed after an injury. The lesion was injected with triamcinolone 10 mg/mL at intervals of 4 weeks. The lesion was flat after four treatments. Early lesions respond better than older lesions.

Keratoacanthoma

Description

- Keratoacanthoma is a rapidly growing, crateriform nodule with a distinctive clinical appearance that is best regarded as a low-grade squamous cell carcinoma (see Chapter 17).

History

- The peak incidence of keratoacanthoma is between ages 50 and 70 years. This tumor is rare before 40 years of age.
- White people with fair complexions are more often affected.
- Typical locations include the face, neck, dorsal hands, and sun-exposed extremities.
- Keratoacanthoma typically does not occur on the palms or soles.
- The lesion erupts rapidly and is often tender.
- Chemical exposure and human papillomavirus have been implicated as causes in animal models, although the role of human papillomavirus in humans is controversial.

Skin Findings

- Solitary flesh-colored to dull-red, crateriform nodules, measuring 0.5 to 2 cm.
- A central keratotic plug or depression conceals a deep keratinous cavity.
- This plug or depression gives the nodule its characteristic volcano-like shape.
- The nodule is firm and tender to palpation or pressure, and it can grow rapidly.
- Keratoacanthoma nearly always appears on sun-damaged skin.
- Three growth phases are described:
  - In the proliferative phase, a solitary papule appears suddenly and then rapidly grows to its maximum size over 2 to 4 weeks.
  - In the mature phase, the lesion is stable in size and appearance for weeks to months; it may appear crateriform if the core has been partially removed.
  - In the resolving phase, the base becomes indurated, the central core is expelled, and the base resorbs, leaving a pitted scar. Resolution may take several months.

Nonskin Findings

- Rare cases of multiple keratoacanthomas have been reported, both as an eruptive (Grzybowski's) form and as a familial adolescent (Ferguson–Smith) form.
- Patients with Muir–Torre syndrome develop sebaceous adenomas, and sometimes keratoacanthomas are present and may be part of the syndrome.
- Such patients should also be evaluated for visceral malignancy and gastrointestinal malignancy.
- Patients on immunosuppressive therapy after organ transplantation are at increased risk for developing keratoacanthomas and invasive squamous cell carcinoma.
- Examination for enlarged lymph nodes should always be performed in this patient population.

Laboratory and Pathology

- The epidermis is expanded with atypical keratinocytes.
- The keratin core is composed of eosinophilic, glassy appearing, atypical, prematurely keratinized cells.

Course and Prognosis

- Left undisturbed, keratoacanthomas may resolve spontaneously or progress into invasive squamous cell carcinoma.
- Although a keratoacanthoma has been historically described as a regressing or

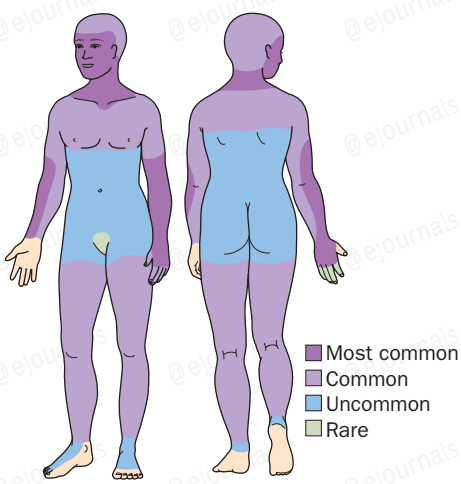

Fig. 16.39 Keratoacanthoma distribution diagram.

Fig. 16.40 A keratoacanthoma type of squamous cell carcinoma can occur anywhere on the body and frequently erupts in sun-exposed areas. The nodule has a smooth, pink border with a hemorrhagic center or crateriform appearance.

Fig. 16.41 A large, dome-shaped, pink keratoacanthoma nodule with central necrosis that can erupt rapidly.

Fig. 16.42 A close-up view of a keratoacanthoma, showing a pink nodule with central necrotic keratin and focal hemorrhagic crust.

absorptive lesion, today most agree that it should be treated as a squamous cell carcinoma.

- Depending on location, the resultant pitted scar that occurs after spontaneous resolution may be cosmetically unacceptable.
- Rarely, keratoacanthomas will attain a size from 1 cm up to 10 cm and are locally destructive.
- Subungual keratoacanthomas can occur and are especially painful and locally destructive.
- Because not all keratoacanthomas regress, they should be regarded as squamous cell carcinomas.

Discussion

- Keratoacanthoma cannot be reliably distinguished from invasive squamous cell carcinoma clinically or histologically.

Treatment

- It is best to presume a diagnosis of squamous cell carcinoma pending biopsy results and clinical follow-up.
- An excisional biopsy or shave biopsy should be performed.
- It is important to excise deep enough to evaluate the dermis for possible invasion.
- Treatment options include complete excision with margins or electrodesiccation and curettage.

Pearls

- Keratoacanthomas characteristically grow rapidly and resemble volcanic craters.
- Radiation therapy is considered for tumors in areas where excisional surgery might result in deformity.
- Intralesional methotrexate and topical 5-fluorouracil have been successful in treating multiple lesions or when tumors are in cosmetically sensitive facial areas.

Fig. 16.43 A small eruptive nodule with central necrosis on the superior helix, characteristic of a keratoacanthoma.

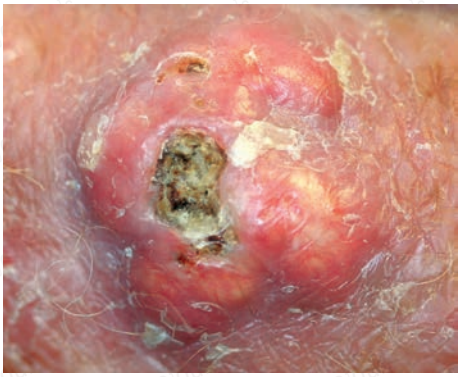

Fig. 16.44 A large keratoacanthoma with multiple coalescing nodules, scattered necrosis, and keratinous debris.

Fig. 16.45 Keratoacanthoma begins as a smooth, dome-shaped, red papule that may rapidly develop a central keratin-filled crater. Lesions grow rapidly. Squamous cell cancers are usually slow-growing tumors.

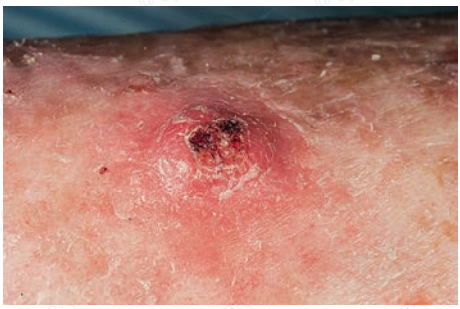

Fig. 16.46 This lesion resembles both a keratoacanthoma and a squamous cell cancer. The pathologist reported features of both tumors. Therefore it was treated as a squamous cell cancer with a wide excision.

Fig. 16.47 Keratoacanthomas are dome-shaped tumors with a central crust. The history of sudden appearance and rapid growth supports the diagnosis. Squamous cell carcinoma may have a similar appearance, but these tumors usually enlarge slowly over many months.

Nevus Sebaceus

Description

- Nevus sebaceus is a distinctive congenital lesion of the scalp, head, and neck and is composed of skin and appendageal components.
- In rare cases, basal cell carcinoma can develop within these tumors.

History

- Nearly all nevus sebaceus lesions are present at birth or appear in early childhood.
- Lesions change clinically and histologically with age, especially during the transition from early childhood to puberty.
- At puberty, nevus sebaceus lesions tend to enlarge, and it is common that it may be noticed for the first time at this point.

Skin Findings

- Nevus sebaceus occurs most commonly as a single lesion on the scalp, forehead, or postauricular area.
- A linear to oval, yellowish to flesh-colored plaque usually measuring 1 to 3 cm in diameter appears.
- The lesion evolves in three stages corresponding to sebaceous gland maturation through childhood, puberty, and adulthood.
- In childhood, the plaque is barely raised and has a velvety surface, is hairless, is pink to tan, and is asymptomatic.
- Around puberty, the plaque tends to thicken, becomes larger and more verrucous, and has a yellow-white and pink speckled appearance. Lesions at this stage are easily traumatized and may be tender.
- The third stage of evolution occurs during adulthood. Approximately 20% of lesions undergo neoplastic change and may develop either benign or malignant tumors of the skin, including basal cell carcinoma.
- Such a change is seen as a new nodule or erosion developing within a previously stable nevus sebaceus.
- The malignancies are low grade and show little tendency to become invasive.

Nonskin Findings

- A triad of nevus sebaceus, epilepsy, and intellectual disability can occur but is very rare.
- This appears to overlap clinically with the linear epidermal nevus syndrome.
- Neurologic evaluation should be considered in these situations.

Laboratory and Testing

- The histopathologic characteristics vary depending on the age of the patient at the time of biopsy.
- In the first few months of life, the sebaceous glands are well developed as a result of maternal hormonal stimulation, although surrounding hair structures are incompletely differentiated.
- Thereafter, and through the rest of childhood, the sebaceous glands are small in size and number; incompletely developed hair structures may be seen.
- With puberty, hormonal influences bring about diagnostic changes. Sebaceous glands mature and increase in size and density. Hair structures remain undifferentiated, and papillomatous epidermal hyperplasia develops. Ectopic apocrine glands may also be found deep within the underlying dermis.
- Appendageal tumors may develop later in life within nevus sebaceus. Each such tumor

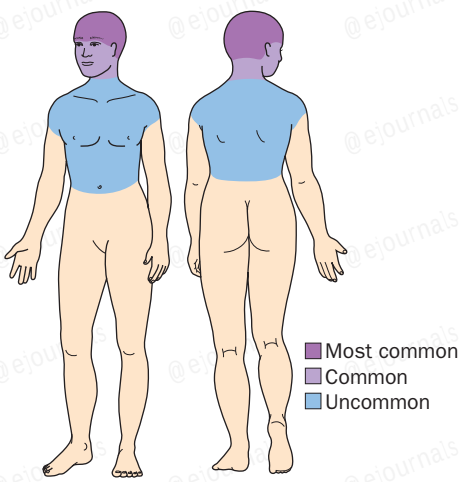

Fig. 16.48 Nevus sebaceus distribution diagram.

has its own histologic pattern. The most common tumor is syringocystadenoma papilliferum, a benign apocrine tumor seen in up to 20% of lesions. Basal cell carcinoma is the second most common tumor and most common malignancy that develops in nevus sebaceus; it occurs in roughly 7% of lesions.

Course and Prognosis

- Nevus sebaceus remains stable throughout childhood and undergoes predictable change at puberty.
- Depending on location, nevus sebaceus can be quite noticeable and even disfiguring.
- Neoplastic change occurs during adulthood with enough frequency to warrant prophylactic excision at puberty in some children.

Differential Diagnosis

- Linear epidermal nevus may share some common histologic features

Treatment

- Excision of the entire lesion is usually recommended in early childhood, but the timing of this procedure remains controversial.

Pearls

- During puberty, there is a massive proliferation of sebaceous glands.
- The nevus develops a verrucous or velvety surface irregularity.
- Nevus sebaceus has a tendency to develop basal cell carcinoma within the nevus after puberty.
- Surgical invasion of nevi should be considered in infancy for certain lesions.
- A larger lesion may be excised in stages without any concern of inducing malignant change.
- Large defects on the scalp are easier to repair during infancy.

Fig. 16.49 Nevus sebaceus. This 12-year-old boy has reached puberty, and the lesion has become thicker. This change at puberty is expected and represents, in part, sebaceous gland and epithelial hyperplasia.

Fig. 16.50 Nevus sebaceus in a 30-year-old man. Two papular areas have developed. Lesions have the propensity to develop into many different tumors. This lesion should be excised.

Fig. 16.51 Nevus sebaceus occurs most often on the scalp. Lesions are also found on the face, neck, and trunk.

Fig. 16.52 Nevus sebaceus. Hormonal changes during puberty stimulate sebaceous gland growth. This causes the velvety smooth surface to become verrucous and nodular.

Fig. 16.53 Nevus sebaceus. Lesions are found on the scalp and face, behind the ear, and on the neck and trunk. This lesion was in the preauricular area of the cheek.

Chondrodermatitis Nodularis Helicis

Description

- Chondrodermatitis nodularis helicis is an inflammatory condition of the helical ear cartilage.
- It is an exquisitely tender papule on the most lateral edge of the helix or antihelix.
- Chondrodermatitis nodularis is due to the degeneration of cartilage, stimulated by trauma.

History

- Chondrodermatitis nodularis helicis usually occurs in people older than 40 years, and the incidence increases with age.
- Men are affected more often than women.
- The helix is involved more commonly in men.
- Lesions on the antihelix are more common in women.
- These variations may relate in part to historical differences among men and women in sun-exposure patterns, occupation, recreational activities, and hairstyles.
- Gender differences in ear structure may also play a role.
- As a rule, most patients are in the habit of talking on the phone and sleeping on the affected side.
- Pressure from a phone or resting on a pillow causes pain.
- This tenderness may force the patient to alter sleeping position and affects the ability to sleep comfortably.
- This condition is less symptomatic during the daytime.

Skin Findings

- The primary lesion is a firm, tender, red to pink papule of 2 to 4 mm with a central keratotic punctum.
- The punctum has firm, adherent crust or scale, resembling a small cutaneous horn.
- The surrounding skin shows actinic damage with atrophy and telangiectasia.
- Occasionally there is more than one lesion, and rarely, they occur bilaterally.
- The universal symptom is pain described as stabbing and sharp. Papules are quite tender to palpation.
- This condition is classically found on the most prominent and lateral portion of the auricle.

Laboratory and Testing

- Skin biopsy reveals both acute and chronic inflammation.
- The epidermis is thinned, with compacted parakeratotic scaling, and often shows central erosion or ulceration.
- There is dermal necrosis with surrounding granulation tissue.
- A deep biopsy may contain underlying degenerated cartilage.

Course and Prognosis

- The etiology of chondrodermatitis nodularis helicis is unclear, although it is believed to be related to focal dermal necrosis due to repetitive trauma.
- Over many years, dermal injury may result from actinic damage, physical pressure, or a combination of both.
- The vascular supply to this tissue is tenuous, and damage is slow to heal.
- Inflammation and granulation tissue reflect attempts at healing the damaged collagen.
- Without treatment, the lesions persist indefinitely.
- Recurrences are common, even after aggressive therapy.

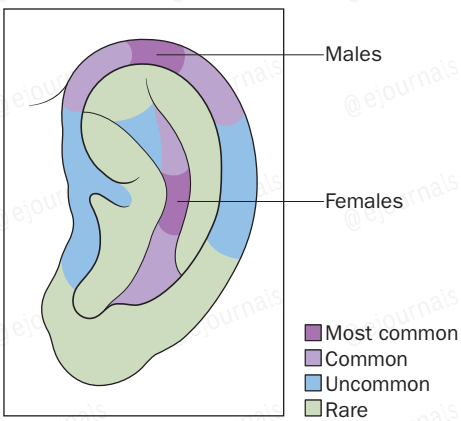

Fig. 16.54 Chondrodermatitis nodularis helicis distribution diagram.

Differential Diagnosis

- Squamous cell carcinoma
- Basal cell carcinoma
- Actinic keratosis

Discussion

- Chondrodermatitis nodularis helicis tends to be painful and is dull red with a poorly defined border.
- Basal cell carcinomas tend to be better defined and have a translucent or pearly appearance.
- Squamous cell carcinomas as a rule tend to be larger, more necrotic, and less tender.
- Skin biopsy should be performed, which is diagnostic.

Treatment

- Any therapy must include efforts to relieve pressure on the affected area to allow for healing.
- Patients who are able to sleep on their backs should be encouraged to do so.
- Pillows should be positioned to minimize pressure on the ear.
- Topical therapy is rarely successful.
- Intralesional steroids can be effective in a minority of cases.
- Patients should expect some residual discomfort after injection.
- Surgical removal of the lesion along with the inflamed cartilage can be curative.
- Shave excision is directed at removing all the inflamed tissue, thus exposing the underlying cartilage.
- Curettage and light electrodesiccation of the base is performed, and the wound is allowed to heal by secondary intention.
- Definitive therapy involves surgical resection of the involved cartilage of the pinna.
- Recurrences are common after any of the previous therapies.

Pearls

- Squamous cell carcinoma closely resembles chondrodermatitis nodularis helicis, and a biopsy to distinguish the two should be performed.
- A deep shave removal biopsy can be both diagnostic and curative.

Fig. 16.55 Chondrodermatitis nodularis helicis. During the active stage, the base may become red and swollen; pain is constant.

Fig. 16.56 Chondrodermatitis nodularis helicis. The lesion, in a typical location, lacks the keratinous plug of a keratoacanthoma or squamous cell carcinoma. Removal of the scale reveals a small central erosion.

Epidermal Cyst

Description

- An epidermal cyst is a firm, subcutaneous, keratin-filled nodule originating from true epidermis.
- It is common, can be found anywhere on the skin, and is usually asymptomatic.
- Patients seek treatment when the cyst expands rapidly or ruptures.

History

- Epidermal cysts arise spontaneously, usually after puberty.
- They occur most commonly on the trunk, postauricular fold, and posterior neck.
- Cysts are usually solitary and frequently develop in areas of friction.
- Unlike pilar cysts, the epidermal cyst wall is fairly delicate and prone to rupture.
- Rupture is followed by an acute foreign body reaction to keratin extruded into the dermis and acute inflammation, giving the appearance of a bacterial infection.
- Although bacteria can be isolated from the cysts, they usually contain normal skin flora.

Skin Findings

- The firm, dome-shaped, pale-yellow intradermal or subcutaneous cystic nodules range from 0.5 to 5 cm in size.
- Cysts are somewhat mobile but are tethered to the overlying skin through a small punctum that often appears as a comedo.
- This punctum represents the follicle from which the cyst developed.
- Inflamed epidermal cysts are warm, red and boggy, and tender on palpation.
- Furuncles have a similar appearance.
- Sterile, purulent material and keratin debris often point toward and drain to the surface.
- If the inflammatory response is brisk enough to destroy the cyst wall, then it is unlikely the cyst will recur.
- More often than not the inflammation subsides, and the cyst recurs.
- Scarring around the cyst often follows, which makes the cyst more difficult to remove.

Nonskin Findings

- Multiple epidermal cysts occurring on the face, scalp, and back should raise suspicion of Gardner's syndrome. This rare, autosomal dominant condition is associated with colonic polyposis and adenocarcinoma of the colon.

Laboratory

- The epidermal cyst is lined with squamous epithelium that appears thinned and flattened.
- The cyst cavity is filled with characteristic layers of cornified lamellated keratin.

Course and Prognosis

- Epidermal cysts grow slowly to a maximum size and tend to persist indefinitely.
- Depending on location, epidermal cysts may be subject to repeated external trauma, inflammatory changes, and rupture.

Treatment

- Epidermal cysts on the face may rupture and lead to scarring.
- The cosmesis of elective surgical excision must be weighed against scar from rupture.
- Such lesions are far more difficult to remove after they have ruptured.
- Asymptomatic epidermal cysts occurring elsewhere do not require treatment.
- Symptomatic or recurrent epidermal cysts should be removed.
- Ruptured, inflamed epidermal cysts should be incised and drained under local anesthesia.

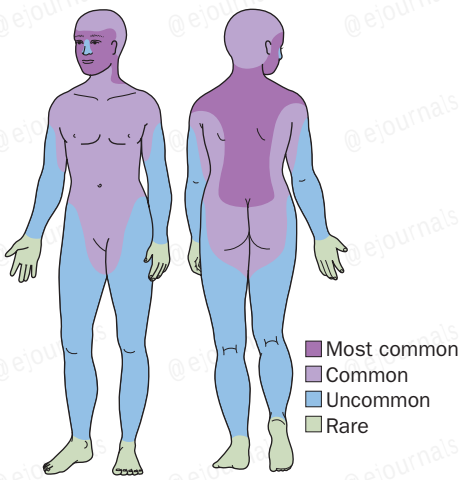

Fig. 16.57 Epidermal cyst distribution diagram.

- Attempts should be made to remove the cyst lining either by curettage or blunt dissection with scissors and forceps.
- Epidermal cysts that have not previously ruptured can be excised easily and completely under local anesthesia.
- Recurrent epidermal cysts that have previously ruptured and scarred are best excised along with the surrounding scar after the inflammation has subsided.

Pearls

- Inflammation after rupture of an epidermal cyst is often suspected and misdiagnosed as infection, but cultures are usually sterile.
- Incision and drainage with curettage do not always completely eradicate epidermal cysts.
- Complete surgical excision with narrow margins is curative.

Fig. 16.58 Yellow-white keratinous, foul-smelling debris extruding from a ruptured epidermal cyst.

Fig. 16.59 Epidermal cyst. A large, tense, inflamed epidermal cyst in the posterior auricular area that has likely ruptured beneath the skin.

Fig. 16.60 Epidermal cyst. Multiple asymptomatic, small and large epidermal cysts on the scrotum.

Fig. 16.61 Grouped yellow subcutaneous nodules on the vulva and in the crural folds, which is a characteristic site for epidermal cysts.

Fig. 16.63 Epidermal cysts vary in size. Lesions of this size will show little tendency to rupture.

Fig. 16.62 An epidermal cyst presenting as a smooth, yellow-white subcutaneous surface on the lateral eyelid.

Fig. 16.64 Epidermal cyst. Ruptured cysts that are close to the skin surface will "point," and the cyst contents will exude onto the skin surface.

Fig. 16.65 Epidermal cyst. Spontaneous rupture of the wall results in discharge of the pale-yellow keratin into the dermis. A tremendous inflammatory response ensues.

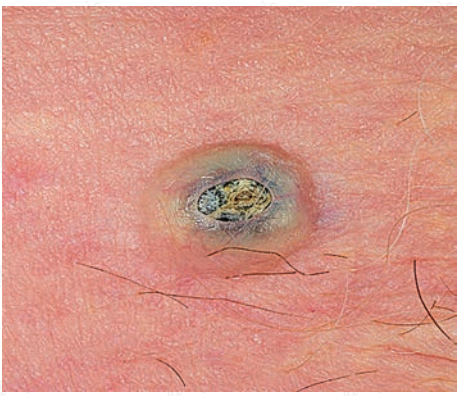

Fig. 16.66 Giant comedones are variants of epidermal cysts. They have a large orifice and are easily removed by incision and drainage. The cyst wall must be removed to ensure that the lesion does not recur.

Fig. 16.67 Epidermal cysts occur commonly on the back of the ear. This cyst spontaneously ruptured and stimulated an intense inflammatory reaction. Incision and drainage relieve the pain and hasten healing. The cyst appears infected, but the inflammation is a foreign body reaction to cyst contents.

Pilar Cyst

Description

- A pilar or trichilemmal cyst is a benign, firm, subcutaneous, keratin-filled cyst originating from the outer root sheath of the hair follicle.
- It is most commonly found on the scalp and can expand and rupture.
- It is sometimes referred to as a "wen."

History

- Pilar cysts are less common than epidermal cysts but are otherwise similar clinically.
- They are autosomal dominantly inherited.
- Roughly 90% of pilar cysts are found on the scalp.
- The remaining 10% occur on the face, neck, back, and scrotum.
- Pilar cysts develop from epithelial cells of the outer root sheath of the hair follicle.
- This epithelium undergoes a different form of keratinization than cutaneous epithelium.
- Pilar cysts almost always develop after puberty and are multiple 70% of the time.
- They persist indefinitely and slowly grow to a stable size unless they rupture.
- Rupture occurs uncommonly, but when it happens, it usually results from external trauma to the head, thus releasing cyst contents into the surrounding dermis.
- A brisk foreign body inflammatory reaction follows and can be painful and resembles a furuncle.

Skin Findings

- Pilar cysts are clinically indistinguishable from epidermal cysts, differing only in pattern of distribution.
- Both present as a firm, slightly mobile subcutaneous nodule ranging from 0.5 to 5 cm.
- No central punctum is seen with pilar cysts, which is found over an epidermal cyst.
- When such a cyst is surgically dissected, the pilar cyst possesses a tough, white-gray wall that is more resistant to tearing than the wall of an epidermal cyst.
- The pilar cyst wall separates easily and cleanly from the surrounding dermis.
- If a pilar cyst ruptures, the area becomes inflamed, red and tender, and boggy on palpation.

Laboratory and Testing

- The histologic characteristics of the pilar cyst are distinct from those of the epidermal cyst.
- The cell wall shows a palisaded arrangement of epithelial cells, with pale cytoplasm but no granular layer.
- The cyst contains concentric layers of homogeneous eosinophilic keratin.

Discussion

- Large cysts may be tender, uncomfortable, and cosmetically objectionable.
- Some cysts are so large and tender that they may interfere with wearing hats and helmets.
- Acute inflammation after rupture is often misdiagnosed as infection and does not require antibiotics.
- Incision and drainage under local anesthesia improve comfort and limit scarring.
- Elective excision before rupture prevents this complication.

Treatment

- Pilar cysts are easily excised under local anesthesia.
- An incision is made over the cyst, exposing the cyst's glossy-white external surface.

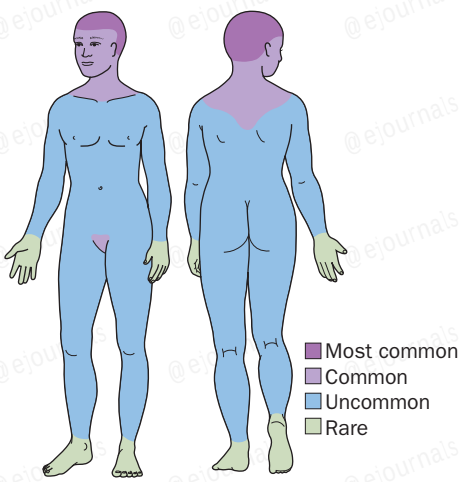

Fig. 16.68 Pilar cyst distribution diagram.

- The cyst wall is freed easily from the surrounding connective tissue by blunt dissection.
- At this stage, smaller cysts may be expressed intact up through the incision by steady, firm pressure on each side of the incision.
- Larger cysts that cannot be expressed in this manner should be incised, and their contents are removed by curettage.
- The incised cyst wall is clamped and (through a combination of gentle traction and pressure on each side of the incision) the now smaller, partially emptied cyst is delivered through the incision.

Pearls

- The term "sebaceous cyst" has been incorrectly applied to this common lesion.
- Pilar cysts are usually found on the scalp and are multiple.
- They are easily removed by surgical excision.

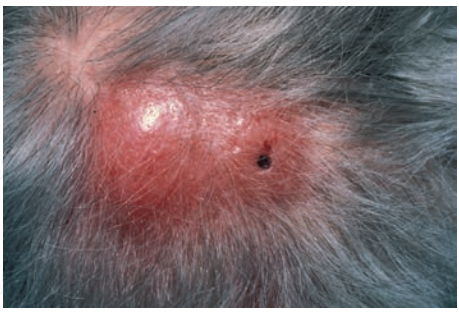

Fig. 16.69 Pilar cyst. This inflamed scalp nodule is rather nondescript and asymptomatic. A punch biopsy wound is seen within the lesion.

Fig. 16.70 A pilar cyst being incised from the scalp, displaying a smooth, white, almost translucent pouch that is usually easily removed with blunt dissection and forceps.

Fig. 16.71 Pilar cysts occur in the scalp and are freely movable.

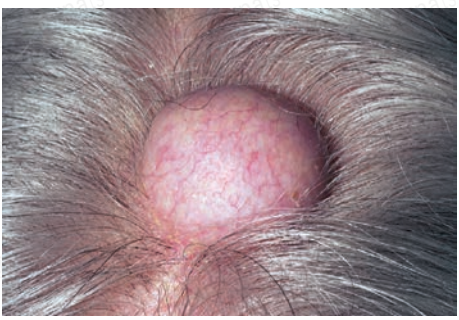

Fig. 16.72 This large pilar cyst has exerted pressure against the skin and has destroyed hair follicles, resulting in a smooth, easily visible scalp nodule.

Sebaceous Hyperplasia

Description

- Sebaceous hyperplasia is a common benign condition consisting of prominently enlarged sebaceous glands on the face.
- These lesions are cosmetically unappealing and can be confused with malignancy.

History

- Sebaceous hyperplasia occurs in both men and women.
- Papules rarely appear before age 30 years but become increasingly more common with advancing age.

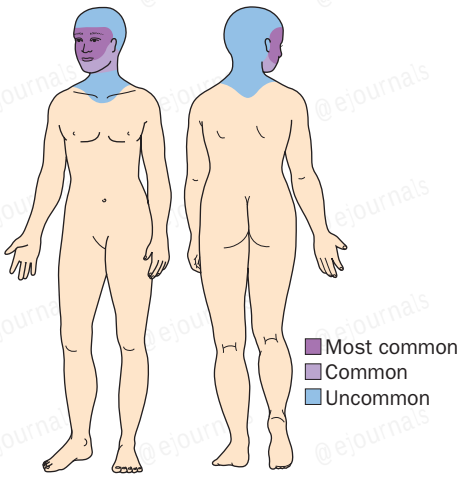

Fig. 16.73 Sebaceous hyperplasia distribution diagram.

- Roughly 80% of patients older than 70 years have at least one such lesion.
- Most lesions represent a single, hypertrophied sebaceous gland, with multiple lobules arranged around a central, enlarged sebaceous duct.
- Lesions occur in all skin types but are more easily seen in lighter skin.
- The etiology of sebaceous hyperplasia is unknown.
- Genetic inheritance almost certainly plays a role.
- Sun damage has been suggested as a contributing factor.
- The lesions are entirely asymptomatic but are persistent.
- Papules can become disfiguring and are mostly of cosmetic concern.
- Older patients are typically concerned that the lesions represent basal cell carcinoma.

Skin Findings

- The lesion begins as a 1- to 2-mm, soft, pale-yellow to skin-colored minimally elevated papule.
- With time the lesion attains a maximum size of 3 to 4 mm and develops a central umbilication.
- Mature papules possess a distinctly yellow-orange color and are more sharply defined from the surrounding skin.
- Papules may be solitary but are more commonly multiple and scattered randomly on the forehead, nose, and cheeks.

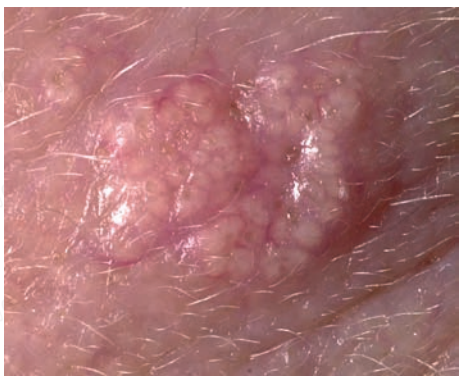

Fig. 16.74 A close-up view of a sebaceous hyperplasia papule, with multiple globules of yellow sebaceous material and a central depression.

Fig. 16.75 Sebaceous hyperplasia. A sebaceous papule with yellow-orange coloration, which is distinct from the more pale color of background skin.

Fig. 16.76 Sebaceous hyperplasia. Individual lesions vary in size, usually scattered in the central face, especially the forehead.

Fig. 16.77 Sebaceous hyperplasia. Yellow-white papules are commonly found on the forehead and cheeks. The central pore is an almost constant feature. Individual lesions may be mistaken for basal cell carcinoma. The vessels in basal cell carcinoma course randomly over the surface.

- An orderly array of fine telangiectasias may radiate outward and between the papules from the umbilication toward the periphery of the papule.
- Because of the smooth surface, sebaceous hyperplasia papules can be misdiagnosed as basal cell carcinoma.

Laboratory

- Skin biopsy confirms the presence of multiple sebaceous lobules of a single sebaceous gland arranged around a central sebaceous duct.
- This duct corresponds to the central umbilication seen clinically.

Discussion

- Individual lesions may be confused with basal cell carcinoma, small keratoacanthoma, or molluscum contagiosum.
- Lesions of sebaceous hyperplasia have an orderly radial arrangement of telangiectasias in contrast to the haphazard distribution of telangiectasias on the surface of a basal cell carcinoma.

Treatment

- Treatment is not required but may be requested for cosmetic reasons.
- Carbon dioxide laser ablation, shave excision, electrodesiccation with curettage, and trichloroacetic acid are all effective ablating procedures, but risk for scarring must be weighed against observing the lesions.
- Photodynamic therapy with aminolevulinic acid and BLU light is effective at "shrinking" sebaceous hyperplasia papules and is repeated annually.
- The sebaceous lobules located within the superficial dermis must be destroyed for the treatment to be successful.
- Reassurance is often all that is needed.

Pearls

- Sebaceous hyperplasia papules can be confused with basal cell carcinoma.
- Clues to the diagnosis of sebaceous hyperplasia are the umbilicated center, radial orderly arrangement of telangiectasias, and the presence of multiple lesions.

Syringoma

Description

- Syringomas are small, benign, firm, skin-colored papules occurring most commonly in women around the eyelids, upper chest, and vulva.

History

- Syringomas are the most common tumor of the intraepidermal eccrine sweat glands.
- Small, benign, appendageal tumors develop after puberty and increase in number throughout young adulthood.
- Women are affected more than men.
- Syringomas most commonly present as multiple small papules around the eyes.
- Lesions are asymptomatic, stable in size and appearance, and persistent.
- The autosomal dominant inheritance of multiple syringomas is well established.
- Syringomas occur with increased frequency in persons with Down syndrome (trisomy 21).
- Facial lesions are of cosmetic concern, and most patients request removal of larger lesions.
- The patient may be concerned that the lesions are cancerous.
- Women seeking evaluation of vulvar lesions may be concerned that the lesions are genital warts.

Skin Findings

- Multiple, skin-colored to yellow, barely raised papules of 1 to 2 mm.
- Papules are most commonly found on the lower eyelids.
- They also occur on the malar cheeks, axillae, anterior chest, abdomen, umbilicus, and vulva.
- Papules are usually symmetrically distributed and asymptomatic.

Laboratory and Pathology

- Increased numbers of dilated, epithelium-lined eccrine ducts are encased in a fibrous stroma.
- These ducts resemble "tadpoles" when cut in cross section.

Course and Prognosis

- Syringomas persist indefinitely and remain small.
- These lesions have no potential for malignancy.

Differential Diagnosis

- Seborrheic keratoses
- Sebaceous hyperplasia
- Angiofibromas
- Common warts
- Flat warts
- Xanthelasma
- Sarcoidosis
- Other appendageal tumors, such as trichoepitheliomas

Discussion

- Trichoepithelioma is a benign appendageal tumor with differentiation toward the hair follicle.
- Like syringomas, trichoepitheliomas also appear after puberty and occur most commonly on the face.
- Multiple lesions can be inherited in autosomal dominant fashion.
- Sebaceous hyperplasia tends to be umbilicated and yellowish and is scattered about the face rather than grouped around the eyes.
- Flat warts occur on the face as small, flat, skin-colored or pink papules.
- Xanthelasma occurs on eyelid skin, especially upper eyelids, and represents cholesterol deposition within dermal macrophages.
- If doubt exists, biopsy should be performed.

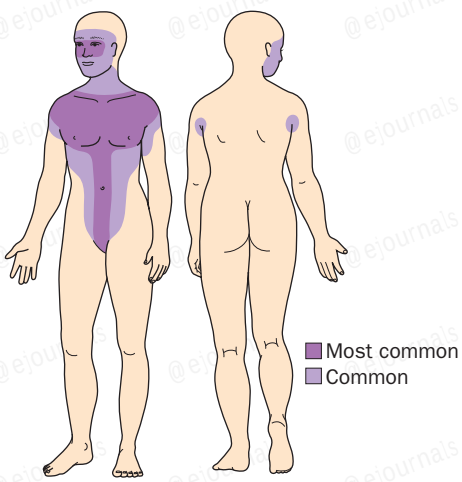

Fig. 16.78 Syringoma distribution diagram.

Treatment

- Syringomas may be removed for cosmetic purposes.
- Electrodesiccation and curettage, cryotherapy, laser surgery, and trichloroacetic acid may be used.
- Sharp dissection or scissor excision of lesions is easily performed under local anesthesia.
- All of these procedures can lead to scarring, so care and precision are warranted.

Pearls

- Syringomas are clinically subtle and can be confused with other dermatoses initially; a biopsy may be needed for confirmation.
- Removal, by any procedure, must be weighed against the risk for scarring.

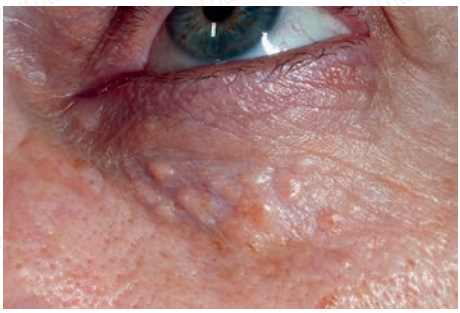

Fig. 16.79 Syringomas are small, pale, white to flesh-colored asymptomatic papules frequently found on the lower eyelids.

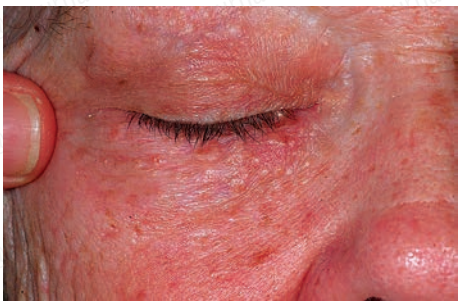

Fig. 16.80 Syringoma. The lower lids are the most common area for finding this appendage tumor. Prominent sebaceous glands may have the same appearance. Lesions may be removed with curved scissors to improve the appearance.

17 Premalignant and Malignant Nonmelanoma Skin Tumors

M. Shane Chapman

Basal Cell Carcinoma

Description

- Basal cell carcinoma is a skin cancer derived from the basal layer of keratinocytes of the epidermis.
- It is the most common cutaneous malignancy and most common cancer in humans.
- If left untreated, basal cell carcinomas will locally invade surrounding skin, destroying underlying tissue.
- Rarely, basal cell carcinomas can metastasize.

History

- Basal cell carcinoma may occur at any age but is more common in later life.
- The highest incidence occurs in people with white or fair skin (types I and II).
- It is less common in Hispanic and Asian skin, and is rare in African Americans.
- Cumulative ultraviolet light exposure is the major risk factor in developing basal cell carcinoma.
- Tumors occur most commonly on the sun-exposed skin of the face, scalp, ears, and neck, and less often on the trunk and extremities.
- There are several clinical variants of basal cell carcinoma: nodular, pigmented, superficial, micronodular, morpheaform, sclerosing, and advanced basal cell carcinomas.
- Each type varies in clinical appearance, histology, and aggressiveness.
- Nodular basal cell carcinoma is the most common type.
- Sclerosing basal cell carcinoma has a higher incidence of recurrence.

Skin Findings

- In general, basal cell carcinomas are pink, violaceous, or pearly-white, sometimes translucent-appearing papules or nodules.
- They may have a smooth surface with overlying telangiectasias.
- The papule or nodule enlarges slowly, flattens centrally, or may develop a raised, rolled border.
- Tumors frequently bleed, become erosive and crusted, and ulcerate in the center.
- Basal cell carcinomas may contain melanin that appears speckled brown, black, or blue in color.
- Curettage demonstrates the characteristically soft texture of the tumor compared with the surrounding normal skin.

Nodular Basal Cell Carcinoma

- The lesion begins as a pearly-white or -pink, dome-shaped papule or nodule with telangiectasia.
- The center may ulcerate and bleed and subsequently accumulates hemorrhagic crust and scale.
- The growth pattern may become irregular, forming an oval or multilobular mass.

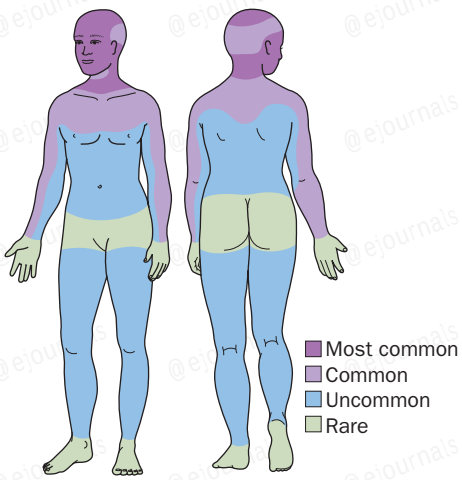

Fig. 17.1 Basal cell carcinoma distribution diagram.

Fig. 17.2 The classical presentation of nodular basal cell carcinoma. A dome-shaped pearly tumor with telangiectasias meanders randomly over the surface.

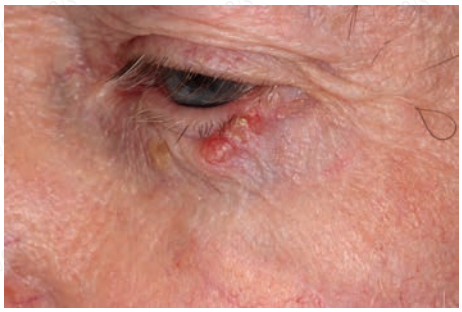

Fig. 17.3 Basal cell carcinoma. This growing pink pearly tumor on the eyelid margin slowly enlarged. A biopsy confirmed the diagnosis, and it was removed by Mohs' micrographic surgery.

Fig. 17.4 Basal cell carcinomas have a characteristic smooth pearly appearance, with superficial telangiectasias.

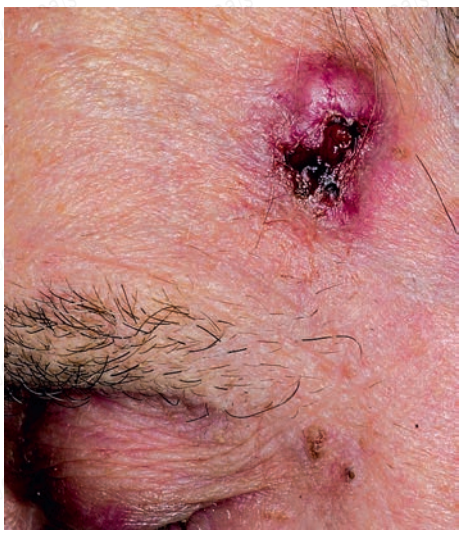

Fig. 17.5 Basal cell carcinoma appearing as a pearly nodule with telangiectasias, with central necrosis and erosion.

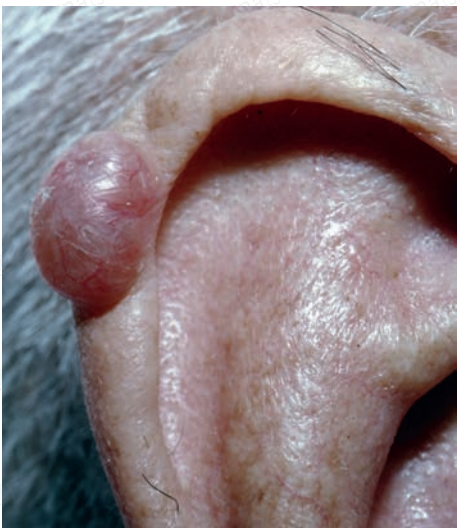

Fig. 17.6 Nodular basal cell carcinomas are common in any location on the head and neck. This nodular basal cell carcinoma is on the sun-exposed helix of the ear.

- These features are characteristic and easily recognized by skin experts.

Pigmented Basal Cell Carcinoma

- This is the clinical equivalent to nodular basal cell carcinoma, with the addition of speckled melanin pigment within.
- The pigment may be sparse or diffuse and resemble malignant melanoma.

Fig. 17.7 Flat, pink, scar-like patch with a shiny border on the helix of the ear, characteristic of a sclerotic basal cell carcinoma.

- The natural history and aggressiveness of the tumor is similar to a nonpigmented basal cell carcinoma.

Superficial Basal Cell Carcinoma

- This is the thinnest and the least aggressive form of basal cell carcinoma.
- These lesions are typically multiple and appear earlier in life, compared with nodular basal cell carcinoma.
- This is found more commonly on the trunk and extremities compared with nodular basal cell carcinoma.
- The lesions are flatter, sometimes atrophic, and not as deeply invasive as the lesions of nodular basal cell carcinoma.
- The borders are less distinct but have the same pearly-pink quality. Stretching the skin may accentuate the raised border.
- The tumor spreads peripherally, sometimes for several centimeters, and invades only after considerable time.
- The circumscribed, round to oval, red, scaling plaques may be confused with eczema, psoriasis, extramammary Paget's disease, or Bowen's disease (squamous cell carcinoma in situ).

Micronodular Basal Cell Carcinoma

- Micronodular basal cell carcinoma resembles nodular basal cell carcinoma clinically, but microscopically there are islands of tumor cells extending beyond the clinical margins.
- Because this histologic variant extends beyond the suspected clinical borders, it recurs more frequently after traditional treatment.

Fig. 17.8 Typical basal cell carcinoma with a pink, smooth, almost translucent surface and diffuse telangiectasias.

Fig. 17.9 Nodular basal cell carcinoma with pink pearly appearance. A small focus of melanin pigment can be seen with dermoscopy.

Fig. 17.10 Basal cell carcinoma. The sun exposed nose is the most common location for a basal cell carcinoma.

Fig. 17.11 Basal cell carcinomas may present as nonhealing ulcers and may appear on any body surface, including the vulva.

Fig. 17.12 Basal cell carcinoma. A smooth pearly nodule with telangiectasias and diffuse gray pigmentation is characteristic of a pigmented basal cell carcinoma. Lesions suspected of being a pigmented basal cell carcinoma should be biopsied to ensure they are not melanoma.

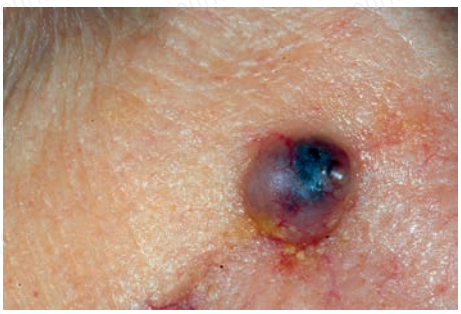

Fig. 17.13 Basal cell carcinoma. Pigmented basal cell carcinoma displaying a pearly nodule with focal area of pigmentation.

Fig. 17.14 Pigmented basal cell carcinoma is a nodular basal cell carcinoma that contains melanin. This lesion has the typical pearly appearance with surface telangiectasia along the periphery and ulceration centrally. Melanoma must be in the differential diagnosis.

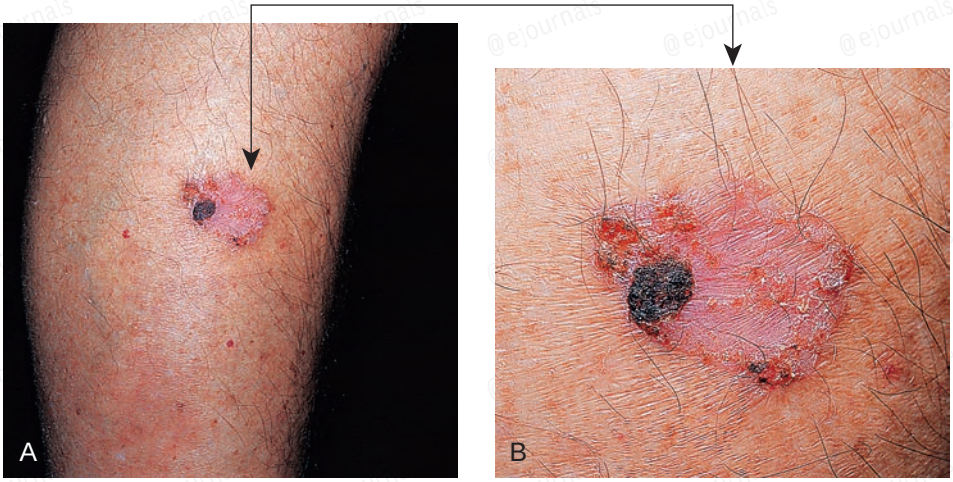

Fig. 17.15 A, B, Superficial basal cell carcinoma. The circumscribed, round to oval, red scaling plaque resembles a plaque of eczema, psoriasis, extramammary Paget's disease, or Bowen's disease. The superficial basal cell carcinoma spreads peripherally, sometimes for several centimeters, and invades after considerable time.

Fig. 17.16 Superficial basal cell carcinoma may be mistaken for eczema, psoriasis, or ringworm. It bleeds and heals in cycles just like a nodular basal cell. The lesion may increase in size to cover very wide areas before the diagnosis is made. Lesions tend to remain superficial but may eventually penetrate deep into the dermis or subcutaneous tissue.

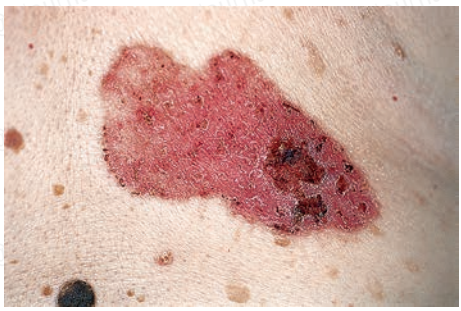

Fig. 17.17 The back is a common place to find superficial basal cell carcinoma. The patient was not aware of the lesion. The sharp border is characteristic. Eczema has a less distinct border. This lesion lacks the silvery scale of psoriasis. The surface of these tumors is often crusted. This lesion was treated with imiquimod cream.

Morpheaform and Sclerosing Basal Cell Carcinomas

- Morpheaform and sclerosing basal cell carcinomas are the most subtle and least common variants of basal cell carcinoma.
- These types of basal cell carcinomas are also the most difficult to eradicate.
- Lesions resemble scar tissue clinically and may appear pale-white to yellow and are waxy on palpation.
- Because of the innocuous appearance of these variants, biopsy and diagnosis are often delayed.
- The margins are indistinct, and tumor cells may extend more than 7 mm from the clinically apparent border.
- Thus, unlike the nodular variant, tumors are more likely to recur after narrow excision.
- Both the morpheaform and sclerosing forms are more aggressive, tend to recur more often, and should be followed more closely.

Advanced Basal Cell Carcinoma

- Advanced or locally advanced basal cell carcinoma are those tumor that are large, have been neglected, and have invaded deeper tissues, such as the ocular mucosa.

- This designation may also be used for tumors located in areas where surgical excision would lead to deformity or functional impairment.
- Treatment options for advanced basal cell cancers include oral therapy with the oral hedgehog inhibitors, vismodigib (Erivedge) and sonidegib (Odomzo), as well as radiation.
- Side effects from this class of medications include muscle spasms and dysguesia or aguesia, which may lead to discontinuation.

Fig. 17.18 A sclerotic basal cell carcinoma with a flat and atrophic scar-like central patch. Because these types of basal cell carcinomas blend into normal skin and are not elevated, there is frequently a delay in diagnosis.

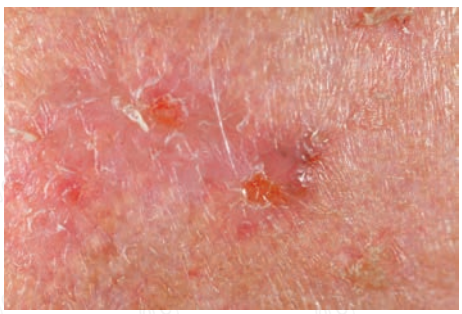

Fig. 17.19 Morpheaform basal cell carcinoma is a waxy, firm, flat or slightly raised, and either pale pink or flesh colored patch that is difficult to discern, even with palpation.

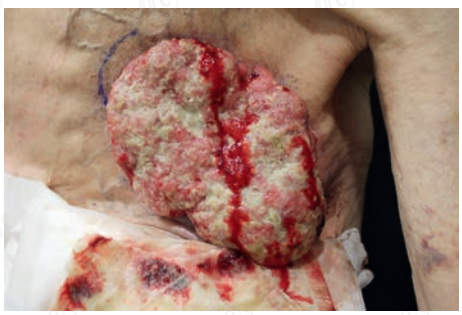

Fig. 17.20 Large, complex, and advanced basal cell carcinomas occur as a result of neglect and delayed diagnosis. Often, patients simply do not seek dermatologic care. This particularly large fungating basal cell carcinoma of the chest wall had invaded underlying muscle, but not the lymph nodes, and was eventually excised.

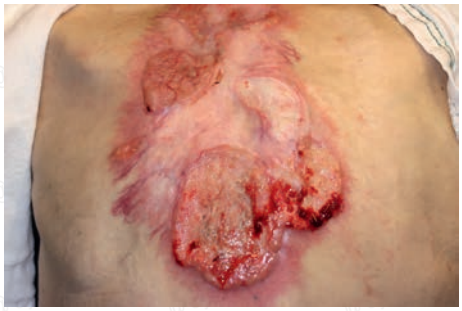

Fig. 17.21 Rarely, basal cell carcinomas can be metastatic. This basal cell carcinoma invaded the vertebral bones, was resistant to radiation and vismodegib, and continued to grow and advance.

Fig. 17.22 Some patients with advanced basal cell carcinoma have numerous basal cell tumors that coalesce, frequently recur, and are difficult to get clear surgical margins. This patient was prescribed vismodegib after several recurrent basal cell carcinoma tumors on the face and scalp.

Basal Cell Nevus Syndrome (Gorlin's Syndrome)

- Basal cell nevus syndrome is an autosomal dominant condition of multiple basal cell skin cancer and multiple associated anomalies of the skin, skeleton, and central nervous system.
- Skin anomalies include multiple basal cell carcinomas appearing early in life and palmar pitting.
- Facial anomalies include a broad nose, heavy brow, and hyperteloric (wide-set) eyes.
- Skeletal anomalies include odontogenic cysts, frontal bossing, hypertelorism, bifid ribs, kyphoscoliosis, and shortened fourth metacarpals, as well as scoliosis and kyphosis.
- Central nervous system anomalies include calcification of the falx cerebri and the development of medulloblastoma.
- Blindness, deafness, and seizures can be a part of the syndrome.
- These patients are a treatment challenge given the increased number of basal cell tumors, young age, functional alteration after surgical excision, and potential for metastatic disease.

Laboratory and Testing

- Histology shows nests of basaloid keratinocyte tumor cells closely distributed in a distinctive stroma in nodular and pigmented basal cell carcinomas.
- Superficial basal cell carcinomas appear as multifocal extensions of the basal layer of the epidermis into the superficial dermis.
- In nodular basal cell carcinomas, there are larger islands of tumor cells within the dermis; tumor islands may be solid or may contain cystic cavities.
- Pigmented basal cell carcinoma is similar to nodular basal cell carcinoma but differs in that tumor islands contain foci or clumps of melanin pigment.
- In morpheaform or sclerosing basal cell carcinomas, collagen-like cords and fine strands of tumor cells are embedded within a fibrous stroma.

Course and Prognosis

- Without treatment, basal cell carcinomas persist, enlarge, ulcerate, and invade and destroy the surrounding structures.
- Inadequately treated basal cell carcinomas recur, often underneath areas of scarring, which may lead to delay in detection.
- In patients who develop one basal cell carcinoma, the annual risk for developing another basal cell carcinoma increases to 5%.

Discussion

- Basal cell carcinomas are rarely life-threatening, but metastases do occur. This is seen more commonly in immunocompromised patients.
- Depending on tumor location, local destruction of normal tissue by the tumor can result in significant impairment. Inadequately treated tumors may extend undetected to destroy large areas of the face, neck, and scalp.

Treatment

- The goal of treatment is eradication of the tumor and return of normal anatomic form and function.
- Treatment of basal cell carcinoma is determined by the size and location of the tumor, by the histologic variant, and the patient's concerns.
- Cosmesis of the wound or defect is an important but secondary concern.
- Clinical aggressiveness correlates with histologic pattern.
- The various treatment options include cryotherapy, curettage, electrosurgery, traditional excision, Mohs' micrographic surgery, radiation, topical chemotherapy and immunotherapy, and photodynamic therapy.
- Inhibition of the transcription of the basal cell carcinoma gene, hedgehog, is now possible with vismodegib (150 mg daily) and sonidegib (200 mg daily).

Cryotherapy

- Some thin basal cell tumors and superficial basal cell carcinomas may be eradicated with aggressive cryotherapy.

Curettage

- Small, discrete nodular tumors with well-demarcated borders can be removed or destroyed by curettage.

- This method is very effective alone or in combination with electrosurgery.

Electrosurgery

- Electrosurgery involves curettage with or without electrodessication of basal cell tumor.
- It is usually performed for well-defined, small nodular basal cell carcinomas and superficial basal cell carcinomas.
- The 5-year cure rate for curettage can approach 92% for primary tumors but is only 60% for recurrent tumors.

Excision

- Outpatient or clinic excision is preferred for well-defined nodular basal cell carcinomas.
- Excision allows confirmation of surgical margins and surgical closure and may be preferred over electrosurgery for some tumors.
- The 5-year cure rate is >90% for primary tumors and 85% for recurrent tumors with this technique.
- This may be the preferred method of removal for nonfacial nodular basal cell carcinomas.

Mohs' Micrographic Surgery

- Mohs' surgery is a highly specialized, tissue-sparing method of tumor excision used for difficult tumors with contiguous growth, especially basal cell carcinomas.
- It is used for recurrent basal carcinomas, for histologically aggressive forms of basal cell carcinomas, and for tumors in anatomically important locations (e.g., around the eyes, nasal ala, mouth, and ears), and tumors with a high risk for recurrence. It is the treatment of choice for sclerotic or morpheaform basal cell carcinomas.

Fig. 17.23 Most basal cell carcinomas have a soft core that is easily removed with curettage.

- The procedure involves debulking the tumor, followed by excision with narrow margins, which is performed in stages.
- Excision is guided by sequential frozen-section mapping in three dimensions.
- This allows histologically confirmed removal of the tumor with the smallest of surgical margin and surgical defect.
- The 5-year cure rates for Mohs' excision approach 99% for primary tumors and 96% for recurrent tumors.
- Mohs' micrographic surgery is useful when tissue sparing is required because of anatomic location, recurrent tumors, and basal cell carcinomas with indistinct borders.

Radiation Therapy

- Radiation may be useful for tumors at difficult sites to treat surgically, such as those on the eyelids, and for patients who are unwilling or unable to tolerate surgery.
- Improvements in computerized treatment models now allow the radiation oncologist to precisely treat a localized tumor with high-dose radiation in fractional doses over several weeks.
- The 5-year cure rate is roughly 90% for both primary and recurrent tumors.
- Cosmesis can be excellent, although expected long-term radiation changes in the treated skin may limit the use of this modality to elderly patients.

Nonsurgical Topical Chemotherapy and Immunotherapy

- Imiquimod 5% cream is an immune response modifier shown to be 85% effective, or better, for superficial basal cell carcinomas. Daily application by the patient at home for 6 weeks results in complete eradication in most cases. Inflammation at the treatment site can be significant; rest periods may be needed.
- Imiquimod for nodular basal cell carcinoma is less well studied; it is slightly less effective for nodular basal cell carcinomas compared with superficial basal cell carcinomas.
- Fluorouracil (Efudex, Carac) 5% cream is a topical chemotherapeutic agent that can also be used to treat superficial basal cell carcinoma.

Photodynamic Therapy

- The combination of a photosensitizing agent, either aminolevulinic acid (ALA) or methyl aminolevulinate (MAL), and addition of a light source, BLU-Light (415 nm) or RED-Light (diode), can be used to treat superficial tumors, which include squamous cell carcinoma in situ and superficial basal cell carcinomas.
- The photosensitizing agent is applied to the skin (tumor) and allowed to be absorbed for 1 to 3 hours.
- The agent is converted into protoporphyrin IX, and the light source excites the porphyrin resulting in a singlet oxygen state, which is damaging to most cancerous cells in the treatment area.

Pearls

- The patient should know that basal cell carcinomas are very common, but rarely life-threatening or trivial.
- Patients must be followed after diagnosis and treatment because tumors may recur and risk for developing another basal cell carcinoma is increased.
- All patients with basal cell carcinomas require follow-up to monitor for the development of new tumors and for recurrence at the treated site, regardless of which treatment is used.
- Basal cell carcinomas may present as nonhealing ulcers and may appear on any cutaneous surface, including the genitalia.
- Morpheaform or sclerotic basal cell carcinomas present as a firm, flat to slightly raised, pale to white papule, which may resemble a scar; it may be missed clinically, but is confirmed histologically. It is more aggressive than other basal cell carcinoma variants and frequently recurs without adequate treatment.

Fig. 17.24 This superficial basal cell carcinoma had been previously treated by desiccation and curettage. Months later, it recurred at the periphery.

Fig. 17.25 The superficial basal cell carcinoma on the left was treated with imiquimod cream applied every other day. Intense inflammation occurred and treatment was stopped. The lesion healed, and there have been no recurrences.

Actinic Keratosis

Description

- Actinic keratoses are very common keratotic lesions with malignant potential.
- They are considered intraepidermal, precursor, or early lesions of squamous cell carcinoma and basal cell carcinoma.
- Lesions are most commonly found in the sun-exposed areas of elderly patients with fair skin types who have had significant sun exposure in their lifetime.

History

- Years of cumulative sun exposure and keratinocyte damage lead to the formation of actinic keratoses.
- Individual lesions become progressively more common after age 40 years.
- Multiple lesions are common in people with fair skin.
- Spontaneous regression and progression to squamous cell carcinoma can occur.
- It is difficult to predict which lesions will progress to invasive cancer, but thick, hypertrophic lesions seem to be more worrisome.
- Approximately 10% of actinic keratoses progress to invasive squamous cell carcinoma over several years.
- Transplant recipients with actinic keratosis must be followed closely because squamous cell carcinoma is more common in these patients, and the potential for metastasis is increased.
- Actinic keratoses are found along with other signs of chronic sun exposure, such as uneven pigmentation, atrophy or thinning, and telangiectasias.
- Lesions are found predominantly on the face, head, neck, and dorsal hands.
- Actinic keratoses initially present as a poorly defined area of redness or telangiectasia.
- Over time, the lesion becomes more defined and develops a thin, adherent, yellowish, or transparent scale.
- At this stage, lesions are sometimes easier to detect by palpation than by observation.
- One may find a discrete sandpaper-like change in skin texture associated with minimal erythema. Patients frequently point out these rough, hyperkeratotic areas to the physician.
- With time, the adherent scale becomes progressively thicker and yellow in color.
- Retained scale may form an elongated keratinous structure or a cutaneous horn.
- Such advanced lesions may be difficult to distinguish from invasive squamous cell carcinoma without skin biopsy, and probably should be treated as a squamous cell carcinoma.
- "Spreading pigmented actinic keratoses" describes actinic keratoses with fine reticulated pigmentation and minimal scaling; they may mimic a solar lentigo or melanoma in situ.
- Lentigo maligna (melanoma in situ) appears as a pigmented patch and occurs most frequently on sun-damaged skin; it may be confused with a spreading pigmented actinic keratosis, and thus a biopsy may be required to establish the correct diagnosis.

Actinic Cheilitis

- Actinic cheilitis is a sun-induced keratinocyte atypia of the lower lip. There is focal crusting and scaling along with blurring of the vermilion border, which appears whitish or gray.
- Actinic lesions in this location can be quite subtle clinically and behave aggressively.
- Like its cutaneous counterpart, actinic cheilitis may progress to overt squamous cell carcinoma of the lip.

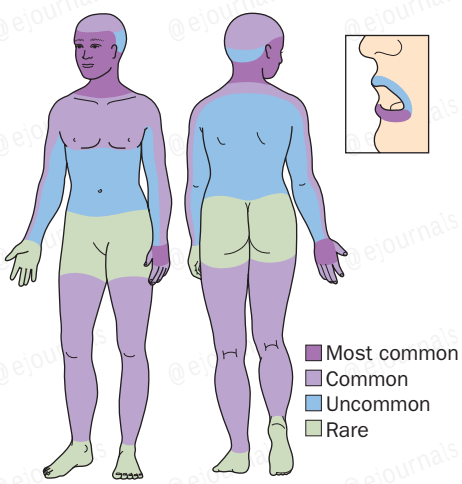

Fig. 17.26 Actinic keratosis distribution diagram.

Fig. 17.27 Actinic keratosis. An early lesion. Scale is yellow, sharp, and tightly adherent.

Fig. 17.28 Actinic keratosis. Numerous lesions are present on the arm. The single dense lesion was excised. The other lesions cleared after a 7-week course of topical 5-fluorouracil.

Fig. 17.29 Actinic keratosis. This typical sun-exposed location on the superior helix has a rough sand-paper feel on palpation.

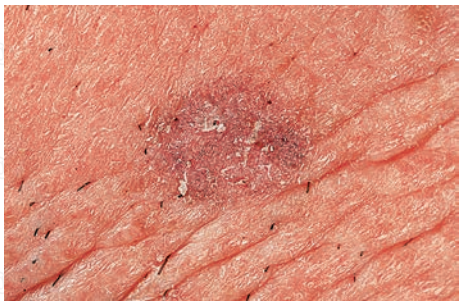

Fig. 17.30 Pigmented actinic keratosis has all of the features of actinic keratosis. There is sharp adherent surface scale and subtle to dense brown pigmentation.

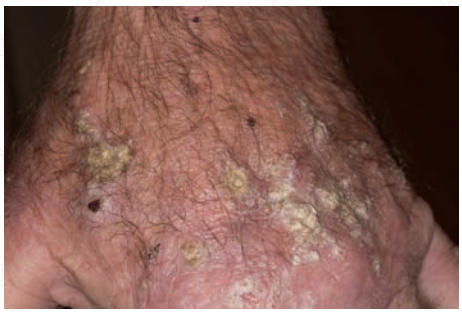

Fig. 17.31 Extremely sun-damaged skin with multiple actinic keratoses that are too numerous to count.

Laboratory and Testing

- Biopsy is often helpful for distinguishing advanced actinic keratoses and actinic cheilitis from invasive squamous cell carcinoma, but this is usually not required because most physicians rely on their clinical expertise.
- The histologic hallmark is a disordered epidermis with intraepidermal keratinocyte atypia.
- By definition, invasion into the dermis of atypical keratinocytes is not seen with actinic keratoses.

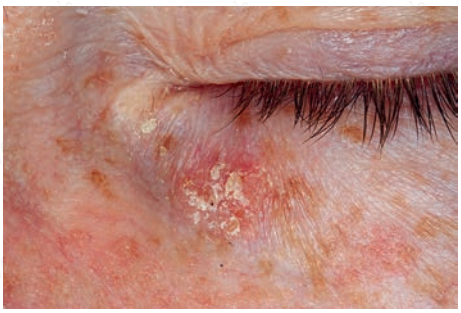

Fig. 17.32 Thick, yellow scale over a pink papule on photodamaged skin is a typical feature of an actinic keratosis.

Fig. 17.33 Actinic keratosis on the nose, with thick yellow adherent scale.

- Similarly, the lesions of spreading pigmented actinic keratosis show keratinocyte atypia with increased pigmentation, whereas atypical melanocytes are seen in lentigo maligna.

Course and Prognosis

- A small percentage of actinic keratosis lesions spontaneously regress with continued sun protection; however, other populations of actinic keratoses progress to squamous cell carcinoma.
- The behavior of an individual lesion cannot be predicted by clinical examination, although hypertrophic lesions may be more prone to progress.
- It has been estimated that 20% of patients with multiple actinic keratoses develop squamous cell carcinoma in one or more lesions.

Fig. 17.34 Actinic keratosis may accumulate dense scale on the surface and become a cutaneous horn. These lesions are excised. Squamous cell carcinoma may have an identical appearance and can be difficult to discern from an actinic keratosis.

- Squamous cell carcinomas that develop on the ear, the scalp, or at the vermilion border are more likely to metastasize than squamous cell carcinomas at other skin sites; thus, actinic keratoses at these sites are more worrisome and should be treated aggressively.

Discussion

- Inflammatory disorders involving the head and neck, such as seborrheic dermatitis and rosacea, can mimic actinic keratoses. Adequate treatment of these inflammatory disorders helps in the prompt recognition and treatment of actinic keratoses.
- Actinic keratoses of the lower legs are frequently multiple, hyperkeratotic, and distributed over a large area.
- Numerous lesions may form on the dorsal hand and forearms, which also have the potential to develop into squamous cell carcinoma.
- Transplant recipients and other immunosuppressed patients pose a difficult treatment conundrum. These patients have a high incidence of squamous cell carcinoma and metastasis. Thus, adequate and aggressive treatment of actinic keratosis and early squamous cell carcinomas is paramount.

Treatment

- The patient with multiple actinic keratoses requires at least annual follow-up, if not more often for some patients who have more extensive sun damage.

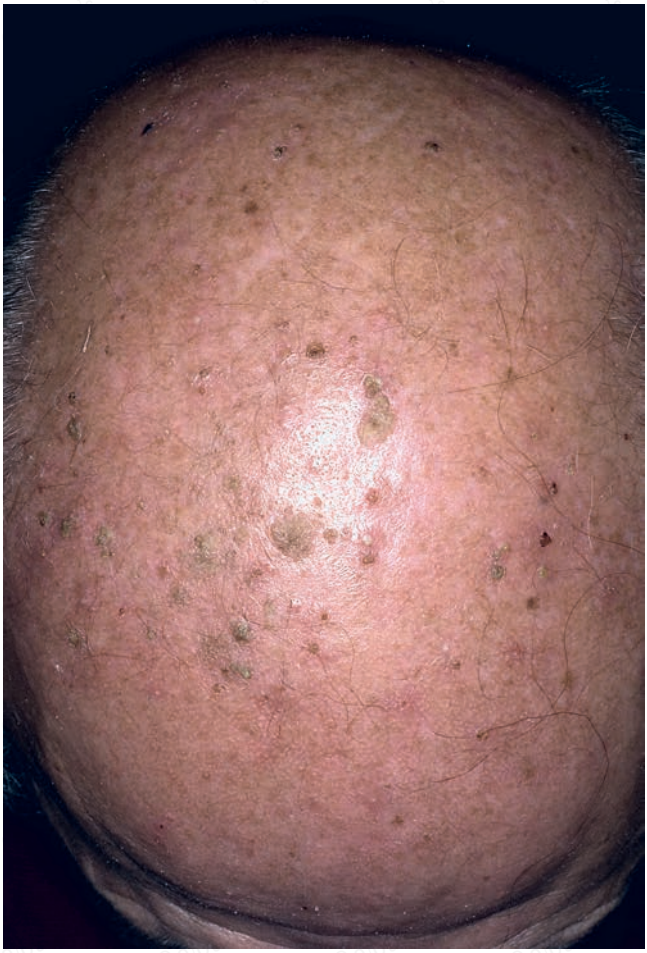

Fig. 17.35 Actinic keratosis. Almost the entire surface of the scalp is covered with thick hypertrophic actinic keratoses. This volume of actinic keratosis is best treated with topical chemotherapy.

Fig. 17.36 Actinic cheilitis presents with erythema and scaling. There is a loss of lip lines, and the skin becomes smooth and eroded.

- Visible or detectable lesions represent a fraction of the total number of atypical keratinocytes actually present.
- Most of the atypia are scattered within sun-damaged skin and below the level of clinical detection.
- These patients will almost certainly develop more clinically apparent actinic keratosis lesions over time.
- Adequate sun avoidance with sun-protective clothing and sunscreens should be encouraged to limit further damage.
- Destruction with liquid nitrogen (cryotherapy) of solitary superficial lesions is the most common method of removal.

- Patients with significant diffuse photodamage or multiple and recurrent lesions present difficult treatment problems.
- It is well documented that patients with numerous actinic keratoses have an increased risk for developing squamous cell carcinoma over time.

Fig. 17.37 This large actinic keratosis had been present for several years, continues to evolve and spread, and is at high risk for transition to squamous cell carcinoma.

Fig. 17.38 This actinic keratosis covers a wide area. It was treated in segments and cleared after three treatment sessions with cryotherapy (liquid nitrogen).

- Topical 5-fluorouracil 5% and 0.5% cream is useful in treating existing, and reducing the number of, atypical keratinocytes in the epidermis and has been the standard in topical, nonsurgical treatment of actinic keratoses.
- Treatment should be tailored for specific areas of the skin, in concentration of the cream, the number of applications per day, and the duration.
- Although treatment of all sun-damaged areas may be appropriate, it is rarely practical to treat large areas at one time. Some patients may prefer instead to treat limited areas on a rotating basis.
- Erythema will appear if actinic keratoses are present. This is followed by warmth, burning, and oozing. Treatment may be stopped before completing the 3-week course if intense inflammation, crusting, or discomfort occurs.
- Patients should be evaluated during the treatment period for discomfort and other complications.
- Imiquimod 5% cream, an immune response modifier, has been shown to effectively treat multiple actinic keratoses when applied three to five times weekly for up to 4 weeks. A new formulation of imiquimod 3.75% cream (Zyclara) is now available.

Fig. 17.39 Actinic keratosis. Topical chemotherapy with 5-fluorouracil. Lesions can become significantly inflamed during the second and third weeks of treatment.

- Inflammatory changes similar to those with 5-fluorouracil occur with imiquimod.
- Photodynamic therapy with either aminolevulinic acid (ALA) or methyl aminolevulinate (MAL) is yet another option for treating extensive diffuse photodamage and multiple actinic keratoses, and allows the physician to treat a large surface area.
- As with the topical therapies, with photodynamic therapy, there is erythema, inflammation, and discomfort, but these symptoms are shorter in duration.
- Electrodesiccation and curettage are also effective and may be necessary for thick lesions.
- All destructive methods ablate the epidermis with minimal effect on the dermis. All have some risk for postprocedure hypopigmentation and scar formation, especially in people with darker skin. This should be clearly explained to the patient before treatment.

Actinic Cheilitis Treatment

- Actinic cheilitis can be treated via several methods and should be tailored to the patient and side-effect profile.
- Cryotherapy can be used to treat actinic cheilitis, for focal or large areas of photodamage of the lip mucosa.
- Carbon dioxide laser vermilionectomy is another option for extensive actinic cheilitis.
- 5-Fluorouracil and imiquimod can also be used on the mucosa (with caution) because the response can be brisk and uncomfortable.
- Application of 5-fluorouracil and imiquimod on the oral mucosa should be less frequent compared with the frequency of skin application and for a shorter duration.
- Although not yet approved by the U.S. Food and Drug Administration (FDA), photodynamic therapy with aminolevulinic acid is effective for actinic cheilitis, either alone or in combination with the treatments presented earlier.

Pearls

- Invasive squamous cell carcinoma can develop from actinic keratosis, especially with thicker, hypertrophic lesions, or lesions not responding to treatment.
- Actinic keratosis lesions of the oral mucosa are especially predisposed to convert to squamous cell carcinoma.
- A biopsy should be considered in any patient who does not respond appropriately to routine actinic keratosis treatment and in actinic keratoses that are recurrent or hypertrophic.
- Some severely actinically damaged patients may require two or three visits per year to adequately treat the numerous actinic keratoses present and prevent progression to squamous cell carcinoma.

Fig. 17.40 Actinic keratosis. A clinical diagnosis of squamous cell carcinoma was made on this thick lesion. Biopsy, however, showed that this was an actinic keratosis with all of the atypical cells confined to the epidermis.

Fig. 17.41 Actinic keratosis on the back of the hands and forearms is often very thick. Differentiating an actinic keratosis from invasive squamous cell carcinoma by inspection may be difficult.

Fig. 17.42 Actinic keratosis. Topical chemotherapy with 5-fluorouracil. Intense inflammation is induced. Thick indurated lesions become inflamed.

Fig. 17.43 Actinic keratosis 3 weeks after treatment with 5-fluorouracil cream. Lesions are inflamed but have not reached the lesion disintegration phase. Treatment was stopped 1 week later when the lesions eroded.

Fig. 17.44 Actinic keratosis 4 weeks after starting treatment with 5-fluorouracil cream. Lesions on the arms are usually thicker and more resistant to treatment. They may require 6 to 7 weeks of treatment to reach the lesion disintegration phase.

Squamous Cell Carcinoma

Description

- Cutaneous squamous cell carcinoma is an invasive, primary cutaneous malignancy arising from keratinocytes of the skin and mucosal surfaces.
- It is most commonly found on the face, head, neck, or hands of elderly patients.
- Lesions may develop from precursor actinic keratoses or may arise de novo.

History

- Squamous cell carcinoma is the second most common form of skin cancer in the United States.
- It comprises 20% of all primary cutaneous malignancies.
- The lifetime risk for developing a cutaneous squamous cell carcinoma is estimated to be between 5% and 15%.
- More than 100,000 new cases of primary cutaneous squamous cell carcinoma are diagnosed in the United States each year.
- Approximately 2500 deaths occur annually from squamous cell carcinoma arising in the skin.
- The incidence of squamous cell carcinoma doubles with each 8- to 10-degree decline in latitude.
- Primary cutaneous squamous cell carcinomas usually occur on sun-exposed skin from years of accumulated actinic damage.
- Nearly 90% of cutaneous squamous cell carcinomas in men and nearly 80% of such tumors in women occur on the face, head, neck, and hands.
- Squamous cell carcinoma on the legs occurs more often in women than in men.
- White patients with fair skin are at greatest risk.
- Although most squamous cell carcinomas are caused by ultraviolet light exposure, other extrinsic factors can play a causal role and include other forms of radiation; chemicals, such as hydrocarbons, arsenic, and tobacco; chronic infections, such as osteomyelitis, chronic inflammation, burns (Marjolin's ulcer), and scars; and human papillomavirus infection.
- Historically, squamous cell carcinoma has been considered as a low-grade tumor with a metastatic rate of less than 1%.
- With the current epidemic of all primary cutaneous malignancies and recent epidemiologic attention, it is clear that squamous cell carcinoma is far more aggressive than previously believed.
- Transplant recipients and other immunocompromised patients develop squamous cell carcinoma much more frequently than the general population, and these tumors can be more aggressive and more likely to metastasize.
- "Conduit spread" refers to the perivascular or perineural extension of tumor cells.
- Ultimately the tumors may metastasize, usually via the lymphatics, to local lymph nodes.

Skin Findings

- As with actinic keratoses, squamous cell carcinomas typically occur on sun-exposed areas.
- Tumors are found within a background of sun-damaged skin with atrophy, telangiectasias, and blotchy hyperpigmentation.
- Early invasive squamous cell carcinoma may have the appearance of a hypertrophic actinic keratosis.

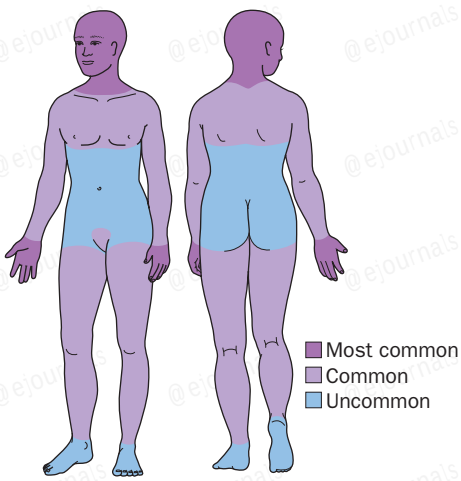

Fig. 17.45 Squamous cell carcinoma distribution diagram.

- The typical lesion has a pink to dull red, firm, poorly defined dome-shaped nodule with an adherent yellow-white scale.
- The untreated lesion becomes larger and more raised, developing into a firm, red nodule with a necrotic, crusted center.
- Removal of the crust reveals a central cavity filled with necrotic keratin debris, sometimes with a foul odor.
- Multiple lesions may appear on the sun-exposed bald scalp, and in some cases lesions may be too numerous to count.
- Actinic keratoses are aggregates of atypical keratinocytes contained within the epidermis.
- At the very least, actinic keratoses represent early squamous atypia, if not definitive squamous cell carcinoma in situ.
- Unlike the lesions of Bowen's disease (squamous cell carcinoma in situ), which show full-thickness involvement, actinic keratoses show partial epidermal cellular atypia, and squamous cell carcinoma by definition shows atypical keratinocytes with invasion into the dermis.

Variants of Squamous Cell Carcinoma

- Actinic keratosis may become thick and hypertrophic, indicating possible progression into squamous cell carcinoma.
- Cutaneous horns may begin as actinic keratosis and progress into squamous cell carcinoma, and should be treated as such.
- Bowen's disease represents full-thickness squamous cell carcinoma in situ that is slow growing, and usually appears as a pink,

Fig. 17.46 Squamous cell carcinoma is commonly found on the ears. The thick verrucous tumor is characteristic of a squamous cell carcinoma.

Fig. 17.47 Differentiating actinic keratosis from squamous cell carcinoma can be difficult. A biopsy demonstrated invasion of atypical squamous cells into the dermis and proved the diagnosis of squamous cell carcinoma.

Fig. 17.48 Squamous cell carcinoma. This large mass had been slowly growing for months. Patients are often not concerned until the skin breaks down and ulcerates, which may lead to bleeding.

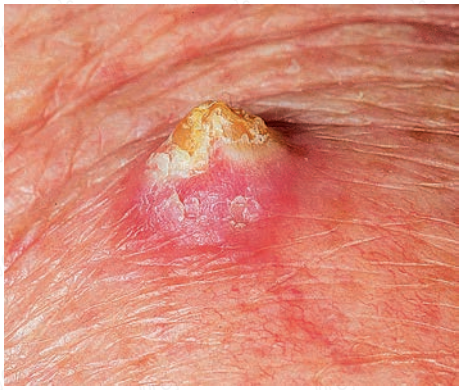

Fig. 17.49 Squamous cell carcinoma retains surface scale. The lesion is called a cutaneous horn if it accumulates a large amount of scale.

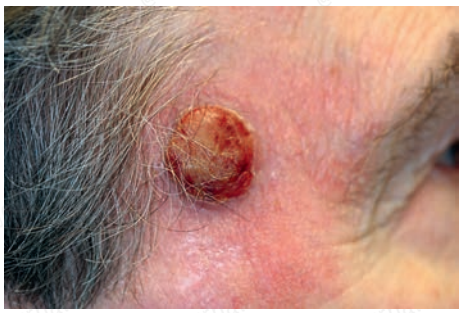

Fig. 17.50 A large yellow-red crusted nodule, characteristic of a squamous cell carcinoma.

Fig. 17.51 This squamous cell carcinoma is multilobular, with hyperkeratotic, verrucous changes superficially and focal areas of hemorrhagic crust.

scaly, well-demarcated patch. If untreated, invasion may ultimately occur.

- Keratoacanthoma is a large, nodular, crateriform, fast-growing nodule with central necrosis, and should now be considered a low-grade variant of invasive squamous cell carcinoma.
- Erythroplasia of Queyrat (squamous cell carcinoma in situ of the penis) is a pink, smooth patch, erosion, or ulcer and may also become invasive. Nodular or ulcerated areas in any tumor suspected of being a squamous cell carcinoma should suggest invasion and thus warrant biopsy. Vulvar squamous cell carcinoma is another variant.
- Squamous cell carcinoma of the oral mucosa is particularly worrisome and prone to metastasis, especially of the lower lip.
- These tumors may arise on an area of actinic cheilitis or chronically sun-damaged mucosa and may develop erosion or ulceration, with an underlying papule or nodule that is usually palpable.

Nonskin Findings

- As previously discussed, squamous cell carcinomas have metastatic potential.
- Metastases are usually to the regional lymph nodes and are detected within 2 to 3 years of cutaneous diagnosis.
- Palpable regional lymph nodes suggest metastatic disease.

Laboratory and Testing

- Skin biopsy and histologic confirmation should be performed for all suspected squamous cell carcinomas.
- Biopsy should include the dermis so that invasion can be assessed.
- Malignant keratinocytes are confined to the epidermis in both actinic keratoses and Bowen's disease.
- In actinic keratoses, malignant cells are usually few in number, are well demarcated, and possess overlying parakeratosis.
- In Bowen's disease, malignant cells are greater in number, are found at all levels of the epidermis, and extend into the epithelium of adnexal structures.
- In invasive squamous cell carcinomas, malignant cells breach the dermoepidermal junction and invade the dermis.
- Tumor cells vary in their degree of differentiation, from well differentiated to poorly differentiated.
- Squamous cell carcinomas with perineural invasion are especially worrisome and more likely to metastasize.

Fig. 17.52 This lower lip tumor expanded quickly and developed a hemorrhagic crust.

- The surgical margins of excised lesions should be examined carefully to ensure complete excision.
- Lesions should be graded as to their degree of differentiation, their depth of invasion, and the presence of perineural invasion.

Course and Prognosis

- The long-term prognosis for adequately treated, nonmetastatic squamous cell carcinoma of the skin is excellent.
- Such patients are at increased risk for developing additional primary skin malignancies, so periodic follow-up is warranted in all patients.
- The metastatic rate of squamous cell carcinomas arising on sun-exposed skin is now estimated to be between 2% and 6%.
- Risk factors for metastasis include the following:
  - Tumor larger than 2.0 cm in diameter, invasion deeper than 0.4 cm, or both.
  - Decreased degree of differentiation of tumor cells.
  - Recurrent tumors.
  - Perineural invasion.
  - Adenoid-producing or mucin-producing variant of squamous cell carcinoma.
  - Immunosuppressed host.
  - Tumor arising in a scar or a chronic wound.
- The risk for metastases is also higher for tumors at specific anatomic sites.
- The metastatic rate for squamous cell carcinomas arising on the lip or ear is estimated at 10% to 20%.

Fig. 17.53 The clinical diagnosis of cutaneous horn is made for any lesion that has accumulated thick scale. The differential diagnosis includes actinic keratosis, squamous cell carcinoma, and wart. Biopsy showed that this lesion was a squamous cell carcinoma.

- The 5-year mortality rate is similar to that of other head and neck tumors.
- Tumors arising within scar tissue have a metastatic rate as high as 30%.

Complications

- Patients on immunosuppressive therapy after organ transplantation are at higher risk for any cutaneous malignancy, especially squamous cell carcinoma.
- Tumors arise with increasing frequency between 5 and 10 years after transplantation.
- Such patients must be followed very closely and their tumors treated aggressively.

Treatment

- The treatment of primary squamous cell carcinoma of the skin involves wide local excision with histologic confirmation of margins.

Fig. 17.54 This squamous cell carcinoma presented as a keratotic nodule with central necrosis and rapid expansion.

Fig. 17.55 Squamous cell carcinoma behind the ear, presenting as a bright-red, tender, weeping hemorrhagic nodule.

- Mohs' micrographic surgery may be useful for specific sites where tissue sparing is of importance.
- Cure by Mohs' micrographic surgical technique assumes contiguous tumor growth, such as that seen in basal cell carcinoma.
- Squamous cell carcinoma may have noncontiguous growth, perhaps rendering Mohs' technique somewhat less effective for squamous cell carcinoma, but still the primary treatment option.
- Palpation of regional lymph nodes is mandatory for all invasive squamous cell carcinoma patients.
- Lymph node biopsy or sentinel node lymphadenectomy is indicated for suspected nodal disease.
- The role of elective node dissection for high-risk lesions is currently under investigation.
- Imaging studies may be warranted for high-risk tumors.
- Radiation therapy may be considered when surgical resection is not feasible or in addition to standard surgical excision, especially if the patient is immunocompromised or if the tumor has perineural invasion or is poorly differentiated.
- Careful follow-up at regular intervals is recommended for all squamous cell carcinomas. Follow-up should include the following:
  - Skin examination and biopsy of new lesions suspicious for malignancy.
  - Visual inspection and palpation of the excision scar for nodularity and other evidence of skin recurrence.
  - Careful examination of the regional lymph node with node biopsy, if indicated, to detect early metastatic disease.
- The sun-exposed lower lip is a common site for squamous cell carcinoma. Palpation may reveal a deep nodular mass. Squamous cell carcinomas originating on the lip, ear, and scalp tend to be more aggressive and metastasize to the regional lymph nodes and beyond.

Bowen's Disease

Description

- Bowen's disease is an intraepidermal or in situ cutaneous malignancy arising from keratinocytes of the skin and mucosal surfaces.
- It is a superficial or in situ variant of squamous cell carcinoma.

History

- Bowen's disease may arise in sun-exposed and sun-protected areas.
- There are multiple etiologies, including ultraviolet light, radiation, chemicals (arsenic), and human papillomavirus.
- Lesions within sun-protected areas may suggest a past history of arsenic exposure or relation to human papillomavirus.
- The onset is insidious, and lesions are persistent and slow growing and evolve over months to years.
- Slow progression may allow the tumor to go undetected and ultimately lead to invasion.
- Lesions are minimally symptomatic and mimic other benign processes, and patients often delay seeking care and diagnosis.

Skin Findings

- Bowen's disease lesions are typically solitary, barely raised, red or pink patches or plaques with dry adherent scale.
- At first glance, the patch or plaque suggests a single sharp-bordered plaque of psoriasis or eczema.
- On closer inspection, the surface scaling is irregular, firm, fissured, and adherent.
- Focal areas of pigmentation are often present and mimic superficial basal cell carcinoma or nevi.
- The border is slightly elevated but usually is not raised or rolled.
- Little if any inflammation is present.
- If untreated, the plaque extends laterally over many years and may become an invasive squamous cell carcinoma.
- Unlike actinic keratoses (partial epidermal thickness), Bowen's disease represents full-thickness replacement of the epidermis with tumor cells.
- Erythroplasia of Queyrat (penile Bowen's disease) is a variant of squamous cell carcinoma in situ occurring on the glans penis or on the foreskin of the penis.
- These lesions are strongly defined red plaques with a moist, glistening surface, which ultimately erode or ulcerate.
- Analogous lesions of squamous cell carcinoma in situ occur on the vulva as well.
- Both of these genital in situ variants of squamous cell carcinoma are associated with human papillomavirus but may not appear as a typical wart or verruca or may even be asymptomatic until the tumor is completely formed.

Nonskin Findings

- Patients with Bowen's disease lesions in sun-protected areas may have a history of arsenic exposure and have associated human papillomavirus colonization.
- Those with a confirmed history of arsenic exposure are at increased risk for lymphoproliferative and gastrointestinal malignancies.

Laboratory and Testing

- Malignant keratinocytes are seen at all levels within the epidermis (full thickness) in a "windblown" pattern.
- Atypical cells extend down along the adnexal epithelium well below the skin surface and do not breach the dermoepidermal junction.

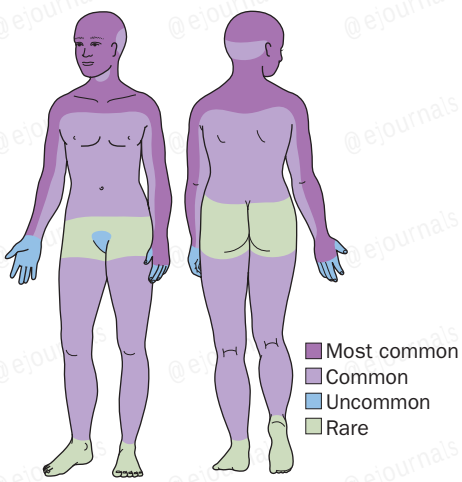

Fig. 17.56 Bowen's disease distribution diagram.

Course and Prognosis

- Bowen's disease is similar to actinic keratoses in that both are intraepidermal lesions containing malignant keratinocytes. However, Bowen's disease is a less common and potentially more aggressive lesion, over time.
- Lesions are full-thickness, extend in continuity with epithelium of adnexal structures, and predictably become invasive.
- Erythroplasia of Queyrat or oral mucosal squamous cell carcinomas have a greater tendency toward invasion and metastases, estimated at 10% to 30%.

Differential Diagnosis

Clinical

- Warts
- Psoriasis
- Localized chronic eczematous dermatitis
- Superficial basal cell carcinoma
- Seborrheic keratosis

Histologic

- Mammary and extramammary Paget's disease
- Amelanotic melanoma

Discussion

- Skin biopsy might be needed to confirm the clinical diagnoses, which is usually diagnostically straightforward.
- Special stains may be required to discriminate between the histologic differential diagnoses.

Fig. 17.57 Bowen's disease is a slowly growing lesion with intraepidermal atypical squamous cells. This plaque looks like psoriasis.

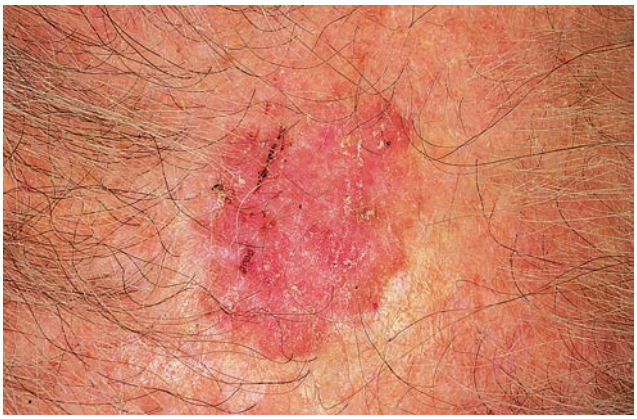

Fig. 17.58 The diagnosis of Bowen's disease is often not made until after biopsy. This plaque looks like an actinic keratosis.

Fig. 17.59 A plaque of Bowen's disease had been present for years. These types of lesions are frequently misdiagnosed as tinea, eczema, or psoriasis, which delays definitive therapy.

Fig. 17.60 Bowen's disease patch that is pink, scaly, and fairly well demarcated. It may be confused with inflammatory disorders, such as eczema and psoriasis.

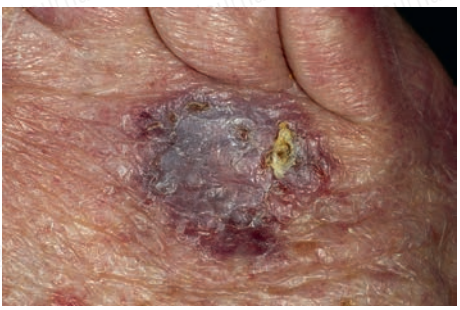

Fig. 17.61 A variant of Bowen's disease with a dark pink to violaceous color change and superficial hyperkeratosis.

Treatment

- Treatment via a procedure with cryotherapy, curettage, excision.
- Topical chemotherapy with 5-fluorouracil cream or immune response modification with imiquimod 5% cream are nonsurgical options.
- Follow-up at regular intervals after treatment.
- Recurrences occur from cells deep in follicular structures and ill-defined lateral margins.
- Any areas suspicious for recurrence should be biopsied or excised without delay.

Pearls

- The borders of Bowen's disease lesions are well defined, and lesions closely resemble psoriasis, chronic eczema, and seborrheic keratosis.
- Some patches of Bowen's disease may be treated with steroids for suspected eczematous dermatitis; therefore, "eczema" that does not respond to steroids may be Bowen's disease.
- Bowen's disease of the penis (erythroplasia of Queyrat) is a moist, slightly raised, well-defined, red, smooth or velvety plaque, and should be treated aggressively given the risk for progression to squamous cell carcinoma over time.

Fig. 17.62 Bowen's disease of the penis (erythroplasia of Queyrat) is a moist, slightly raised, well-defined, red, smooth or velvety plaque.

Fig. 17.63 Analogous to Bowen's disease of the skin, erythroplasia of Queyrat grows very slowly and has the potential for degeneration into squamous cell carcinoma.

Leukoplakia

Description

- Leukoplakia is a descriptive clinical term reserved for white patches or plaques occurring on the mucosal surfaces.
- Diagnostic possibilities range from benign hyperkeratosis to squamous cell carcinoma.

History

- Leukoplakia is a common, sometimes chronic condition of the oral mucosa.
- It occurs more frequently in men than in women.
- It usually appears after age 40 years, and the prevalence approaches 8% after age 70 years.
- Most lesions are asymptomatic, can fade over time without treatment, or develop into cancer.
- More than 80% of people with leukoplakia use some form of tobacco.

Skin Findings

- Leukoplakia begins as a single small, well-defined, translucent to white, slightly elevated papule or patch.
- Individual, untreated lesions may resolve completely, recur, or progress.
- Multiple papules may coalesce into larger plaques over time.
- Uneven hyperkeratosis or small erosions may develop.
- Focal red areas or discrete papules termed *erythroplakia* may develop within plaques, giving a speckled appearance.
- Lesions may occur anywhere on the oral mucosa but are most commonly found on the buccal mucosa and lower lip.
- Unlike the white patches of mucosal candida or thrush, leukoplakia is not easily removed or rubbed off the mucosa.

Laboratory and Testing

- The clinical appearance is often more striking than the histologic characteristics.
- There is a sparse, mixed inflammatory infiltrate in the submucosa, but histology is benign or nondiagnostic in many cases.
- Squamous cell carcinoma in situ is the most common malignancy seen.

Course and Prognosis

- "Leukoplakia" is a descriptive clinical term, not a definitive diagnosis.
- The term is often misused to designate a premalignant condition.
- "Premalignant" implies epithelial dysplasia and impending conversion to a true malignancy.
- Thus, "leukoplakia" is best used to describe a chronic, whitish, oral plaque in which dysplasia has yet to be shown by biopsy.
- There is always a risk for malignant transformation with time. This is especially true for lesions on the ventral tongue and floor of the mouth.
- Factors that favor or promote malignant transformation include tobacco, alcohol, ultraviolet light, and some human papillomavirus infections, as well as an immunocompromised state of the host.
- When malignant change is demonstrated histologically, a definitive diagnosis of squamous cell carcinoma is made.
- Invasive squamous cell carcinoma of the mucosa carries a much greater risk for metastasis than squamous cell carcinoma arising in skin.

Differential Diagnosis

- Candidiasis (thrush)
- Oral hairy leukoplakia
- Frictional hyperkeratosis
- Lichen planus
- White sponge nevus
- Squamous cell carcinoma

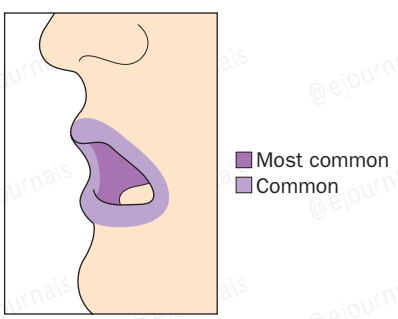

Fig. 17.64 Leukoplakia distribution diagram.

Discussion

- Oral candidal lesions are less adherent to the mucosa, easily removed with scraping, and the diagnosis can be confirmed by potassium hydroxide examination.
- The presence of *Candida* organisms does not exclude the possibility of an underlying condition, including malignancy.
- Oral hairy leukoplakia occurs in patients with advanced disease caused by HIV. White linear patches occur most commonly on the lateral aspect of the tongue. Epstein–Barr virus is the causal agent.
- Frictional hyperkeratosis results from surface trauma, dental appliances, or bite abnormalities.
- Lesion location correlates with the source of the trauma.

Treatment

- Patients who use tobacco products should be encouraged to stop.
- Any area of leukoplakia that changes, especially if there is a change into a nodule or erythema, should be biopsied.
- Localized areas of epithelial dysplasia may be treated by cryosurgery, electrocautery, or topical 5-fluorouracil. Combinations of these therapies are sometimes used.
- Areas demonstrating squamous cell carcinoma, either in situ or invasive, are best treated with surgical excision. Close clinical follow-up, including lymph node examination, is required.
- Indefinite clinical follow-up is required after treatment to detect recurrence. This includes inspection of other areas of the oral mucosa as well as regional lymph node examination.

Pearls

- For leukoplakia, close clinical follow-up is necessary, and oral biopsy for suspicious lesions should not be delayed.

Fig. 17.65 Leukoplakia. The white papules are slightly elevated and well demarcated, and they show little tendency to extend peripherally.

Fig. 17.66 Leukoplakia extending along the middle mucosal lower lip.

Fig. 17.67 Degeneration to carcinoma develops in less than 20% of all patients with leukoplakia and takes 1 to 20 years. All lesions should be palpated; a firm mass indicates squamous cell carcinoma.

Cutaneous T-Cell Lymphoma

Description

- Cutaneous T-cell lymphoma is a distinct helper T-cell lymphoma of the skin.
- It may eventually invade the lymph nodes, peripheral blood, and internal organs.
- The disease most often evolves through several stages or variants: mycosis fungoides, patch, plaque, and tumor stages.
- Some patients may have only one stage present or may have all four stages present simultaneously at the time of diagnosis.
- Sézary's syndrome is the leukemic form of cutaneous T-cell lymphoma that may develop de novo or may evolve from classical plaque/patch cutaneous T-cell lymphoma.

History

- Cutaneous T-cell lymphoma is rare, occurring in 0.5 cases per 100,000 people.
- Men are affected twice as often as women.
- Many cases develop slowly and indolently, not presenting with recognizable features of cutaneous T-cell lymphoma.
- Most cases are diagnosed in the fifth and sixth decades of life.

Skin Findings

- "Parapsoriasis" is a term that some use to describe the premycosis fungoides phase of cutaneous T-cell lymphoma.
- Clinically, this entity appears similar to patch-stage cutaneous T-cell lymphoma, but is not diagnostic of cutaneous T-cell lymphoma histologically. Some feel this is a precursor stage of cutaneous T-cell lymphoma, but this is controversial. This early or premycosis fungoides stage may not respond to topical steroids and may persist for months or years.
- Clinically, this early stage shows scattered pink to red scaly patches that poorly demarcated and resemble eczema or psoriasis.
- Patch-stage cutaneous T-cell lymphoma can be confused with eczema, but one sees a sharply demarcated red to pink, scaly, atrophic, mottled, telangiectatic eruption with cutaneous T-cell lymphoma.
- In the plaque stage, dusky red to brown, slightly elevated patches and plaques are seen. The disease in this form is often located on the "bathing trunk" area—the buttocks, hips, and upper thighs. The inner aspects or flexural areas of the upper arms and legs are often involved early. The shape of the individual plaques is variable; round, oval, arciform, or serpiginous patterns occur, occasionally with central clearing. The extent varies from a few isolated areas to a major portion of the skin.
- In the tumor stage, red-brown expanding nodules proliferate; they are variable in size, and ulceration may occur.
- In Sézary's syndrome, erythroderma and generalized scaling occur; the palms and soles may be thickened; and alopecia and ectropion are common.
- Infiltration of the entire skin produces a red, thickened skin with increased scale (exfoliative dermatitis) or without scale (erythroderma).
- Peripheral node enlargement and generalized pruritus are also common with Sézary's syndrome.

Nonskin Findings

- The initial workup should include clinical evaluation for peripheral lymphadenopathy and hepatosplenomegaly.
- Systemic and organ involvement is an ominous sign and affects the staging of the disease.

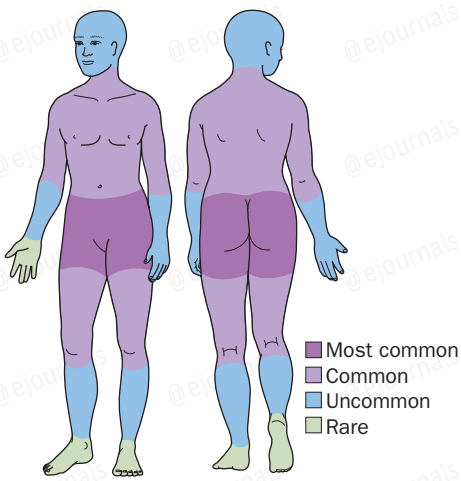

Fig. 17.68 Cutaneous T-cell lymphoma distribution diagram.

Laboratory and Testing

- Despite new and improved laboratory diagnostic methods, recognition of the physical signs of the disease by the clinician is still the most sensitive method of detection.
- Baseline laboratory tests include complete blood count with a peripheral smear examination for Sézary's cells, liver function tests, blood urea nitrogen levels, creatinine level, lactate dehydrogenase (LDH) level, and chest radiograph. The results are usually normal in the patch and plaque stages. The CD4/CD8 count and ratio are done in generalized patch/plaque disease and in higher stage disease.

Fig. 17.69 Cutaneous T-cell lymphoma. Early lesions are red with subtle scale or fine wrinkles. They persist for months with little peripheral extension and are often diagnosed as eczema and treated with topical steroids.

Fig. 17.70 Cutaneous T-cell lymphoma. At plaque stage, numerous elevated annular tumors have become diffuse and generalized.

- Histologically, cutaneous T-cell lymphoma lesions exhibit a superficial and deep, band-like and perivascular lymphocytic infiltrate with collections of lymphocytes (Pautrier's microabscesses) within a thickened epidermis. The infiltrate becomes mixed, with lymphocytes, eosinophils, and plasma cells, as the plaque stage progresses. Some lymphocytes are atypical, having a large hyperconvoluted or cerebriform nucleus (Sézary's cells).
- Multiple large biopsies or excisional biopsies may be necessary. It may be best to perform a fusiform excision and bisect the specimen along the longer longitudinal length of the excision.
- Molecular studies may be diagnostically helpful in the early stages or in clinically atypical cases; polymerase chain reaction and Southern blotting may reveal T-cell receptor gene rearrangement, indicating the presence of a clonal population of cells.

Differential Diagnosis

- Atopic dermatitis
- Eczematous dermatitis
- Allergic contact dermatitis
- Psoriasis
- Drug eruption

Fig. 17.71 Cutaneous T-cell lymphoma. Lesions tend to remain fixed in location and size, and the margins are sharply delineated.

Fig. 17.72 Cutaneous T-cell lymphoma. A red psoriasis-like eruption and an atrophic, mottled, telangiectatic surface, referred to as *large-patch parapsoriasis* or *poikiloderma vasculare atrophicans*, occur.

Treatment

- Treatment is stage dependent and includes the degree of skin, nodal, and internal organ involvement.
- A referral to a dermatologist or oncologist is recommended for staging and treatment.
- In the patch and plaque stages, topical steroids, topical chemotherapy (nitrogen mustard, carmustine), psoralen plus ultraviolet A, ultraviolet B, total-body electron-beam therapy, interferon, denileukin, topical or oral retinoids, or a combination of these therapies is used.
- In the tumor stage, spot radiation and interferon and combinations of the chemotherapeutic treatments mentioned previously can be effective.
- In erythroderma or Sézary's syndrome, extracorporeal photopheresis, interferon, oral retinoids, methotrexate, prednisone, and cyclophosphamide or combinations of these therapies are used, along with supportive care if needed.
- More advanced disease may require combinations of the previously mentioned treatments, depending on the stage and immune status and health of the patient.

Fig. 17.73 Cutaneous T-cell lymphoma. Generalized patches that can degenerate into necrotic and ulcerated plaques and tumors.

Course and Prognosis

- In general, the course and prognosis relate to the stage of the disease.
- The early cutaneous T-cell lymphoma and patch stages can last for many years without progression to tumor development, adenopathy, or internal organ involvement.
- Some patients simply have smoldering inflammatory changes resembling eczema that are kept under control with topical steroids; at the other end of the spectrum are progression to the plaque and tumor stage and visceral organ infiltration.
- Necrosis and ulceration of plaques and tumors are common in progressive cases.

- Cutaneous T-cell lymphoma may eventually infiltrate the lymph nodes and viscera; if there is no response to treatment, cutaneous T-cell lymphoma can be fatal.

Fig. 17.74 Cutaneous T-cell lymphoma. Tumors develop from pre-existing plaques or erythroderma, or they may originate from red or normal skin.

Fig. 17.75 Cutaneous T-cell lymphoma. Tumors vary in size. Some become huge.

Pearls

- Early-stage (or premycosis fungoides) and patch-stage cutaneous T cell lymphoma closely resemble eczema, and may not be recognized or misdiagnosed for months or years.
- Eczematous dermatitis that does not respond to traditional therapy may represent early or premycosis fungoides.
- A biopsy can be diagnostic of cutaneous T-cell lymphoma with appropriate clinical correlation.
- However, multiple biopsies (3–6) over several months may be required to confirm this diagnosis.

Fig. 17.76 Cutaneous T-cell lymphoma. Large plaques of tumor-stage mycosis fungoides.

Paget's Disease of the Breast

Description

- Paget's disease of the breast or nipple is a rare, distinctive cutaneous presentation of intraductal carcinoma of the breast.

History

- Paget's disease of the breast is one of the more common cutaneous presentations of breast cancer but represents less than 5% of all cases of breast cancer.
- It occurs almost exclusively in women.
- The incidence increases with age, reflecting the incidence of breast cancer.
- It has an insidious onset, lasting months to years, usually in the fourth to sixth decades of life.
- It may be asymptomatic, and when it is symptomatic patients complain of localized itching, irritation, and discomfort.
- It is often misdiagnosed as "nipple eczema."
- Paget's disease of the breast should be suspected in cases of "nipple eczema" that do not improve with eczema treatment.
- Patient denial or delay in seeking care results in a delay in the biopsy, diagnosis, and treatment.

Skin Findings

- The lesion is a pink to red, sharply demarcated, irregular-shaped, scaly patch or plaque on the areola or nipple.
- The process appears eczematous, but will not respond to topical steroids.
- The patch or plaque is indurated and has sharp margins, which remain relatively fixed for weeks.
- Malignant cells migrate through the epidermis, and the disease becomes initially apparent on the areola and, at a much later date, on the surrounding skin.
- The nipple, areola, and surrounding breast skin may be involved.
- Most often it is unilateral, but it can be bilateral.
- Initially induration is minimal. Over time, induration, infiltration, and nodularity develop.
- An underlying breast mass is palpable in roughly 50% of cases.
- Eventually there is local destruction of the nipple and areola with retraction, and discharge.

Nonskin Findings

- Underlying intraductal carcinoma is usually diagnosed in the affected breast.
- The contralateral breast should also be examined.
- The risk for cancer in the second breast is increased in patients who already have cancer in one breast.
- The regional lymph nodes are rarely palpable unless a palpable breast mass or superficial ulceration is present.

Laboratory and Testing

- Skin biopsy confirms the presence of Paget's cells, which are large, round, pale, mucin-producing cells within the epidermis.
- Paget's cells are scattered among the normal-appearing keratinocytes, often displacing cells along the basal layer.
- Unlike keratinocytes, Paget's cells lack intracellular bridges and are positive for periodic acid–Schiff and carcinoembryonic antigen.
- These special stains help distinguish mammary Paget's disease from melanoma and Bowen's disease.
- Deep biopsy may show continuity with an underlying intraductal carcinoma.

Course and Prognosis

- Mammary Paget's disease is caused by the intraepidermal spread of malignant cells from an underlying intraductal carcinoma of the breast.
- The prognosis is determined by breast cancer staging and therapy.
- The 5-year survival rate exceeds 90% when neither a breast mass nor regional lymph nodes are palpable.
- The 5-year survival rate is roughly 40% when an underlying breast mass is palpable.

Differential Diagnosis

- Nipple eczema
- Erosive adenomatosis of the nipple
- Bowen's disease
- Superficial basal cell carcinoma

- Tinea and candidal infections
- Contact dermatitis and other causes of eczematous dermatitis

Discussion

- Eczematous dermatitis is usually pruritic and should respond to topical corticosteroids.
- Adenomatosis of the nipple is a benign condition best confirmed by biopsy.
- Yeast and fungal infections should be confirmed by potassium hydroxide examination and should improve with topical antifungal therapy.
- The presence of yeast or a fungus does not exclude the possibility of Paget's disease.
- Skin biopsy should be performed for lesions of the nipple and areola that do not respond to topical therapy.

Treatment

- Breast and nodal examination is indicated for all patients with Paget's disease of the breast.
- Skin biopsy should be performed to confirm the diagnosis, followed by mammography.
- A referral to a breast cancer surgeon should be made for further evaluation of any palpable breast mass.

Pearls

- Skin biopsy should be performed for all dermatoses involving the nipple that do not respond to topical therapy or that persist for more than 1 month.

Fig. 17.78 Paget's disease of the breast. Malignant cells migrate through the epidermis, and the disease becomes initially apparent on the areola and, at a much later date, on the surrounding skin.

Fig. 17.77 Paget's disease of the breast. The disease begins insidiously in one breast, with a small area of erythema on the nipple that drains serous fluid and forms a crust.

Fig. 17.79 Paget's disease of the breast. The process appears eczematous, but the plaque is indurated and has sharp margins, which remain relatively fixed for weeks.

Extramammary Paget's Disease

Description

- Extramammary Paget's disease is a rare, easily overlooked, intraepidermal malignancy involving the anogenital or axillary skin.
- It may be related to an underlying occult urogenital tumor, or may be a primary cutaneous tumor.

History

- Extramammary Paget's disease is an intraepidermal adenocarcinoma that occurs in areas of apocrine glands.
- It may be divided into two groups based on the source of the underlying primary adenocarcinoma.
- Most cases represent adenocarcinoma in situ with extension of primary adenocarcinoma in situ from adnexal structures.
- A minority of cases reflect an intraepidermal spread of tumor cells from noncutaneous adenocarcinomas, via local or lymphatic spread.
- Urogenital and rectal carcinomas are the most common origins of noncutaneous adenocarcinoma associated with extramammary Paget's disease.
- These include transitional cell cancer of the urethra and bladder, as well as carcinomas of the cervix, vagina, Bartholin's glands, and prostate.
- Local contiguous or regional lymphatic spread of these carcinomas leads to intraepidermal invasion.
- Extramammary Paget's disease is rare before age 40 years, occurring more often in men than women.
- In men, it occurs more commonly in the crural folds, scrotum, penis, anal, and perianal skin.
- It occurs more commonly on the vulva and perineum in older women.
- It may extend to involve the lower abdomen, inguinal folds, buttocks, and thighs.
- Other rare sites include the axillae, ears, and eyelids.
- The patient may complain of itching and irritation, but rarely pain.
- The lesions slowly and relentlessly increase in size.

Skin Findings

- A red to white-gray patch or plaque with a velvety or scaly surface is typical of this disease.
- The patch or plaque is sharply demarcated and has irregular borders, some with mild superficial scale.
- The lesion may appear inflamed, eczematous, or lichenified.
- Light scale to heavy crusting, erosion, and serous exudate may occur.
- It is most often unilateral, but can be bilateral at presentation.

Nonskin Findings

- Depending on site of origin, the noncutaneous primary adenocarcinoma may be visible and palpable.
- Regional lymph nodes are usually not palpable early in the course of the disease, but this should be evaluated.

Laboratory and Testing

- The histologic features of extramammary Paget's disease are identical to those of mammary Paget's disease.
- Skin biopsy reveals an underlying adnexal adenocarcinoma and Paget's cells within the epidermis.
- Like mammary Paget's disease, extramammary Paget's disease stains positive to periodic acid–Schiff and carcinogenic antigen.

Course and Prognosis

- Unlike Bowen's disease, in extramammary Paget's disease dermal invasion and regional metastases appear to occur earlier in the disease course.
- Therefore, after the diagnosis is made, aggressive treatment and close follow-up are indicated.
- Less than 25% of all patients with extramammary Paget's disease have an underlying noncutaneous malignancy.
- Of those patients with extramammary Paget's disease and underlying malignancy, 25% eventually die of the underlying malignancy.
- The most common sites of metastases are the inguinal and pelvic lymph nodes,

followed by the liver, bone, lungs, brain, bladder, prostate, and adrenal glands.
- The prognosis depends on the site of the primary adenocarcinoma, its clinical stage, and therapy.

Differential Diagnosis

Clinical
- Eczematous dermatitis
- Lichen simplex chronicus
- Intertrigo
- Candidiasis
- Tinea
- Bowen's disease

Histologic
- Bowen's disease
- Melanoma
- Squamous cell carcinoma in situ

Treatment

- The surrounding clinically normal-appearing skin may also be involved.
- Local excision with obvious clear margins of the involved areas is standard.
- Although the lesion appears to be sharply defined clinically, histologic confirmation of margins is vital.
- There is a high recurrence rate, even after excision with apparently appropriate margins.
- There may be benefit from Mohs' micrographic excision, either as an initial procedure or for recurrences.
- Dissection of palpable regional lymph nodes may be warranted in certain cases.
- Radiotherapy and adjuvant imiquimod 5% cream are additional options for difficult cases or recurrent disease.

Fig. 17.80 Extramammary Paget's disease. The disease appears as a white to red, scaling or macerated, infiltrated, eroded, or ulcerated plaque, most frequently observed on the labia majora and scrotum.

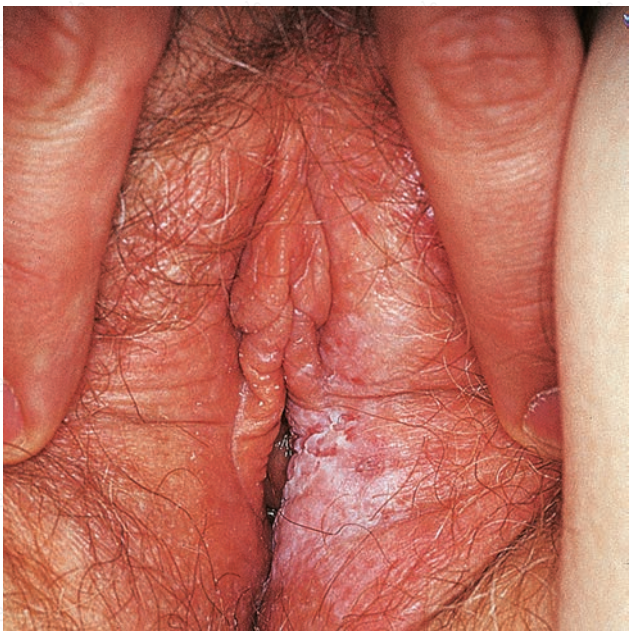

Fig. 17.81 Extramammary Paget's disease. A white eroded plaque with ill-defined borders on the labia.

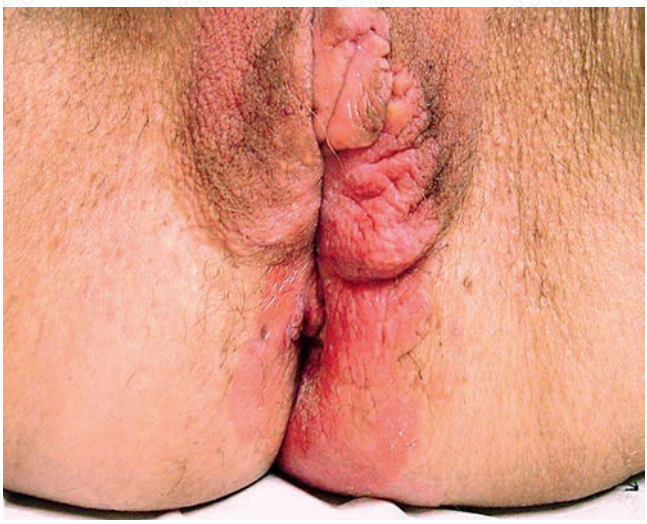

Fig. 17.82 Extramammary Paget's disease. Three biopsies were taken before malignant cells were demonstrated at the periphery of this chronic ulcer at the base of the vulva.

Cutaneous Metastasis

Description

- A cutaneous metastasis from an internal tumor is an uncommon sign of malignancy.
- Certain types of internal tumors have a predilection for certain regions of the body, but usually do not have any specific clinical features.
- A degree of suspicion is usually required to make diagnosis of cutaneous metastasis.

History

- Cutaneous metastases occur in 1% to 10% of all cancer patients.
- Detection of cutaneous metastasis is an ominious sign and may alter disease staging and therapy.
- Cutaneous metastases presenting as the first sign of underlying occult malignancy are uncommon but occur most frequently with tumors of the lung, kidney, and ovary.
- More commonly, cutaneous metastases are a sign of extranodal disease in people with known underlying malignancy.
- Cutaneous metastases may herald recurrence in a patient with a prior history of malignancy.
- Excluding lymphomas, the origin of primary tumors metastasizing to skin reflect the underlying gender differences of primary tumors.
- Common primary sites of men and women with cutaneous metastases are shown in Table 17.1.

Table 17.1 The Most Common Sites of Origin for Cutaneous Metastasis

In Women	
Breast	70%
Colon and rectal	10%
Melanoma	5%
Ovaries	4%
Lungs	4%
In Men	
Lungs	25%
Colon and rectal	20%
Melanoma	13%
Oral cavity	12%

- Metastases to the skin usually occur via lymphatic or hematogenous spread, and rarely by direct extension of the tumor.

Skin Findings

- The origin of cutaneous metastasis can be best divided by region of the metastasis.
- The abdominal wall is the most common site for tumors presenting as metastatic disease.
- About 75% of skin metastases in male patients occur on the head and neck, anterior chest, and abdomen.
- About 75% of skin metastases in female patients occur on the anterior chest or abdomen.
- Scalp metastases in men tend to be from the lung or kidney and present early in the disease.
- Scalp metastases in women tend to be from the breast and present late in the disease.
- Facial and scalp metastases tend to be from oral squamous cell carcinoma, renal cell carcinoma, lung cancer, or breast cancer.
- Eyelid metastases tend to be from breast cancer or melanoma.
- Neck metastases are more often a direct extension from deep nodes from the lung, oral squamous cell carcinoma, or breast carcinoma.

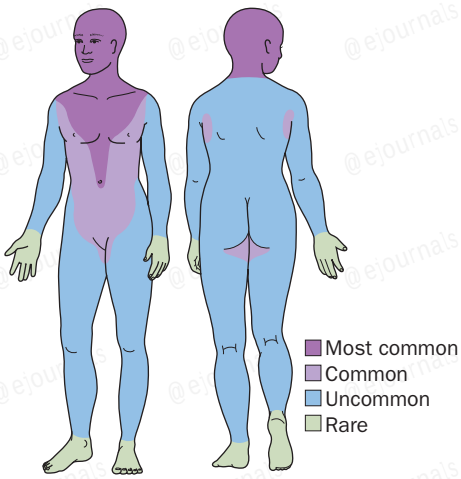

Fig. 17.83 Cutaneous metastasis distribution diagram.

- Most cutaneous metastases do not have a distinct clinical appearance.
- Some of the more common cutaneous metastasis may present as red to violaceous, discrete, firm, painless nodules.

Breast Cancer

- About 70% of all cutaneous metastases in women are related to breast cancer.
- Skin involvement occurs in 24% of breast cancer cases and is the presenting sign 3.5% of the time.
- Metastasis to the skin occurs by direct extension or via lymphatics.
- Most sites of breast metastasis occur at the site of mastectomy, anterior chest, or axillae.
- Occasionally, back, scalp, and the head and neck can be involved.
- The most common presentation of cutaneous breast metastasis is an aggregate of discrete, firm, nontender, skin-colored nodules that appear suddenly, grow rapidly, attain a certain size (often 2 cm), and remain stationary.
- Other distinct clinical patterns of metastatic breast cancer include inflammatory, telangiectatic, erysipeloid, *en cuirasse*, alopecia neoplastica, and zosteriform.
- Inflammatory or telangiectatic metastatic carcinoma resembles erysipelas in the anterior chest but without fever or tenderness.
- In telangiectatic metastatic carcinoma, the violaceous papulovesicles resemble lymphangioma circumscriptum, which may be pruritic and resemble vasculitis.
- *En cuirasse* metastatic carcinoma is a diffuse morphea-like induration or tightening of skin or "encasement in armor"–type changes, that begins as scattered, firm, papules that eventually coalesce.
- In nodular metastatic carcinoma, multiple firm papules or nodules, which may be ulcerated, appear on the anterior chest.
- Alopecia neoplastica has asymptomatic, noninflammatory, circular areas of alopecia, likely due to hematogenous spread.
- In Paget's disease of the breast, there is a sharply defined plaque of erythema and scaling on the breast, suggestive of eczema, but the eruption is persistent. It is usually unilateral but may be bilateral.

Colon and Rectal Carcinoma

- Colon and rectal carcinoma is the second most common source of skin metastases in both genders.
- It usually presents late in the disease course, when the diagnosis is already known, and when the primary colon or rectal carcinoma has already spread to other organs, especially the liver.
- The abdomen, perineum, and previous surgical incision sites are the most common sites of spread.
- It may also present as inflammatory metastatic carcinoma of the inguinal folds or as a chronic cutaneous fistula.

Melanoma

- Melanoma is the third most common cause of metastasis to the skin.
- Melanoma typically invades the liver, lungs, and brain but may also present at distant cutaneous sites.
- Skin is the most common primary site of melanoma, followed by ocular and mucosal sites.
- Metastatic melanoma to the skin usually appears as round blue or gray papules or nodules, sparsely grouped.
- Rarely, metastatic melanoma to the skin may be nonpigmented or amelanotic and appear pink or red.
- There are cases of systemic or metastatic melanoma without a known primary cutaneous melanoma (Table 17.2).

Lung Carcinoma

- Historically, lung carcinoma is more common in men than women.
- It can present as a localized cluster of pink to violaceous nodules, most often on the anterior chest or abdomen.
- Spread from the lungs to the skin may be from blood vessels or from direct extension from a lung biopsy conduit or previous surgical scar.

Table 17.2 Common Primary Sites of Origin for Men and Women With Cutaneous Metastases

Site of Origin	In Women	In Men
Breast	69%	2%
Colon and rectal	9%	19%
Melanoma	5%	13%
Lung	4%	24%
Connective tissue sarcoma	2%	3%
Cervix	2%	3%
Pancreas	2%	2%
Oral cavity squamous cell carcinoma	1%	12%
Bladder	1%	2%
Ovary	4%	—
Prostate	—	1%
Salivary glands	2%	2%
Skin squamous cell carcinoma	—	1%
Kidney	—	6%
Thyroid	—	1%
Stomach	—	6%
Liver	—	1%

Renal Cell Carcinoma

- Renal cell carcinoma makes up 7% of all cutaneous metastases.
- It most commonly presents on the head and neck region.
- Metastatic renal cell carcinoma may appear as a well-circumscribed, red or bluish nodule with prominent vessels.

Oral Squamous Cell Carcinoma

- Oral squamous cell carcinoma metastatic to the skin usually occurs in men with a known primary tumor.
- It presents as multiple red or pink nodules on the head, neck, and scalp region.
- It may be difficult to discern metastatic disease from primary squamous cell carcinoma of the skin.
- Palpation of the cervical lymph nodes may help assess the source of the primary tumor and the staging process.

Neuroblastoma

- Neuroblastoma is the most common neonatal tumor that metastasizes to the skin.
- About 30% of patients with congenital neuroblastomas have subcutaneous and cutaneous metastases.
- It presents on the skin as multiple firm, mobile, blue subcutaneous nodules that blanch when stroked and may show a "blueberry muffin–like" appearance.
- The neoplasm also metastasizes to the liver, lymph nodes, and bone marrow.

Lymphomas

- Cutaneous metastases occur in 6.5% of all patients with lymphoma.
- A skin lesion is the presenting sign in 5% of patients and the first sign of extranodal disease in 8% of patients.
- These are firm, raised, smooth, red or violaceous nodules and plaques that may open, drain, and ulcerate.
- It may be difficult to discern primary lymphoma arising in skin from metastatic disease and true cutaneous T-cell lymphoma.

Leukemia Cutis

- Leukemia cutis often precedes or is concurrent with a diagnosis of systemic leukemia.
- Lesions are seen in 25% to 30% of infants with congenital leukemias and may precede other manifestations of leukemia by up to 4 months.
- Leukemia cutis may appear in many clinical forms: macules, papules, ecchymoses, purpura, or ulcerations.
- The chloroma variants are rare but have a distinctive greenish color due to myeloperoxidase within the lesions.
- Myeloblastomas may occur in acute myelocytic leukemia.
- Mucocutaneous involvement is more common in monocytic leukemias, with involvement ranging from papules to plum-colored nodules and gingival infiltrations.

- Adult T-cell leukemia involves the skin in 75% of patients.

Nonskin Findings

- The primary tumor site and potentially other noncutaneous metastases are usually detectable by imaging studies.

Laboratory

- Skin biopsy confirms the malignancy and sometimes the malignant cells of primary tumor origin.
- Tissue-specific immunohistochemical stains may be of value in cases in which the primary site is not obvious.
- Fresh, unfixed specimens are optimal for specialized immunohistochemistry and molecular studies.

Course and Prognosis

- The prognosis of each internal malignancy is determined by the tumor type, extent of disease, and available treatment options for the primary tumor.
- In general, metastatic disease has a very poor prognosis.

Discussion

- In some cases, excision of symptomatic or disfiguring skin metastases can significantly improve a patient's quality of life.

Treatment

- Therapy is directed by the underlying malignancy.

Pearls

- Biopsy should be performed for any new nodule in an old scar or any new nodule in a new scar if a malignancy was the reason for the procedure or excision.
- Besides discrete nodules or plaques, the second most common pattern of cutaneous metastasis is inflammation with erythema, edema, warmth, and tenderness. This inflammation may not resemble metastatic disease initially, causing a delay in diagnosis.

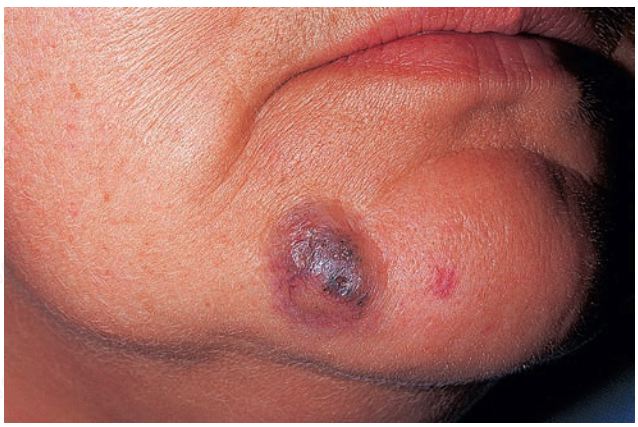

Fig. 17.84 The most common presentation of cutaneous metastasis is an aggregate of discrete, firm, nontender, skin-colored nodules that appear suddenly, grow rapidly, attain a certain size (often 2 cm), and remain stationary.

Fig. 17.85 The second most common pattern of cutaneous metastasis is inflammation with erythema, edema, warmth, and tenderness.

Fig. 17.86 Cutaneous metastasis. Grouped pink nodules from metastatic breast carcinoma (male).

Benign Melanocytic Neoplasms and Melanoma 18

James G. H. Dinulos

Acquired Melanocytic Nevi (Moles)

Description

- Acquired melanocytic nevi are common benign skin tumors composed of melanocyte-derived nevus cells.

History

- Acquired melanocytic nevi are more common in whites than Asians and Africans.
- Numbers of acquired melanocytic nevi peak in early adolescence, slowly increase in number until age 30 years, and then regress in elderly people.
- Genetic factors, as well as environmental influences, such as increased ultraviolet radiation (e.g., natural sunlight and tanning), determine the number of acquired melanocytic nevi.
- Other factors, such as skin injury, immunosuppression, hormones, and medications, have been associated with increased numbers of acquired melanocytic nevi.
- Skin disorders, such as lichen sclerosis and epidermolysis bullosa, may be associated with acquired melanocytic nevi.
- Most acquired melanocytic nevi occur on sun-exposed areas, although Asians and Africans are more likely to develop nevi on acral sites (e.g., palms, soles, and nails) and the conjunctiva.
- Most white adults have between 12 and 20 acquired melanocytic nevi.
- Acquired melanocytic nevi are asymptomatic, although they may be irritated by clothing or external trauma.

Skin Findings

Junctional Nevi

- Junctional nevi are brown to tan macules with preserved skin epidermal markings.
- Acquired melanocytic nevi on the palms, soles, and genitalia are usually junctional nevi.

Compound Nevi

- Compound nevi are firm brown papules that may have a smooth or papillomatous surface.

Intradermal Nevi

- Intradermal nevi are skin-colored to tan papules with a smooth surface.

Nevus Spilus

- Nevus spilus is a speckled tan to brown patch with sharply demarcated borders, similar to a café-au-lait macule.
- There may be brown papules within the nevus spilus.

Blue Nevi

- Blue nevi are solitary blue to black macules and papules, commonly found on the head and neck.

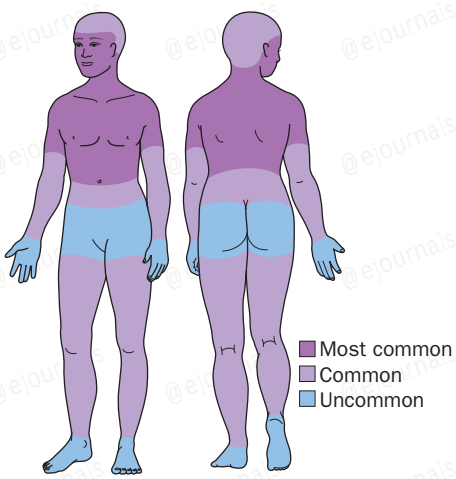

Fig. 18.1 Acquired melanocytic nevi distribution diagram.

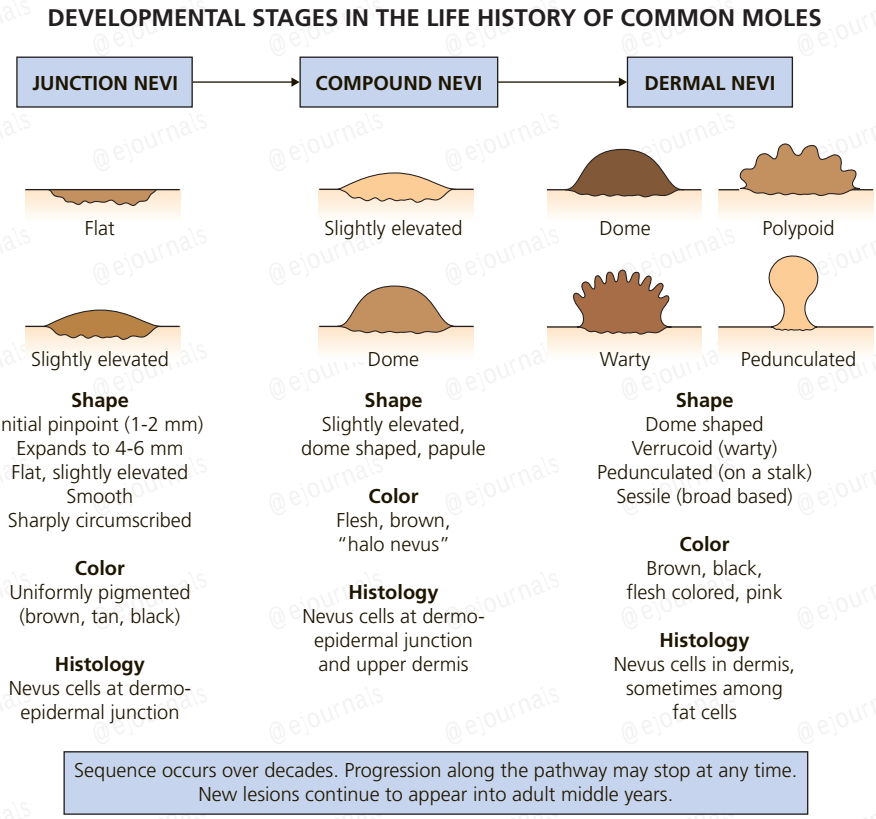

Fig. 18.2 Developmental stages in the life history of common moles.

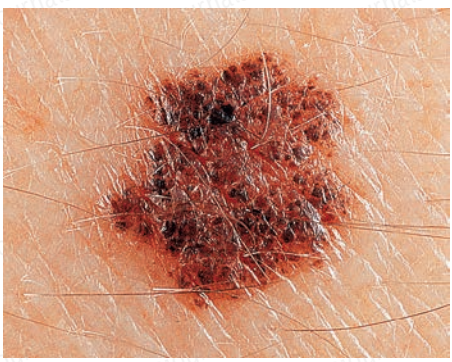

Fig. 18.3 Junctional nevi: flat, uniform hyperpigmented macules.

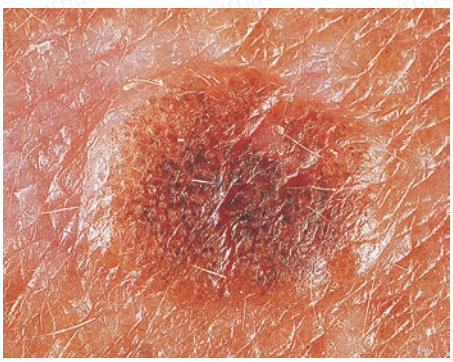

Fig. 18.4 Compound nevi: hyperpigmented papules.

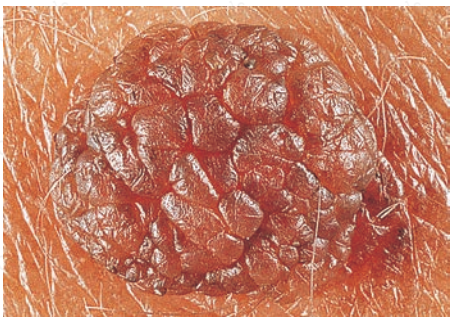

Fig. 18.5 Intradermal nevi: skin-colored papules.

Fig. 18.6 Nevus spilus: light brown patch with dark brown macules. Nevus spilus rarely develops melanoma but is difficult to detect change because of the dark speckles.

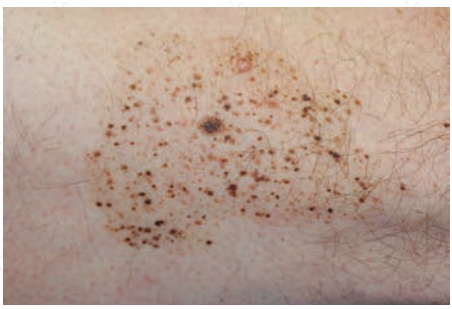

Fig. 18.7 Nevus spilus with background café-au-lait macule containing small benign nevi. These lesions are benign and do not change appearance.

- The dark color is attributed to heavily pigmented melanocytes in the deep dermis.

Spitz Nevus (Spindle and Epithelial Cell Nevus)

- Spitz nevus is a pink to red-brown dome-shaped smooth papule.

Fig. 18.8 Blue nevi. Dark blue due to pigment deeper in the dermis.

Fig. 18.9 Spitz nevus. They are considered benign, but if they are irregular in color or if they grow, they should be removed.

- Histologically, Spitz nevi may be difficult to differentiate from melanoma.
- Spitz nevi are more common in children.

Halo Nevi

- Acquired melanocytic nevi with a rim of depigmentation are called *halo nevi*.
- An immune response to the melanocytes is responsible for the halo.
- Vitiligo is associated with halo nevi.
- Halo nevi occur primarily during adolescence.
- Wood's lamp examination is helpful to evaluate for associated vitiligo.

Recurrent Nevi

- A recurrent nevus is an irregularly pigmented macule or papule associated with a scar from a previous procedure.
- Recurrent melanocytic nevi appear similar to melanoma.

Laboratory

- A skin biopsy should be performed on suspicious pigmented lesions.

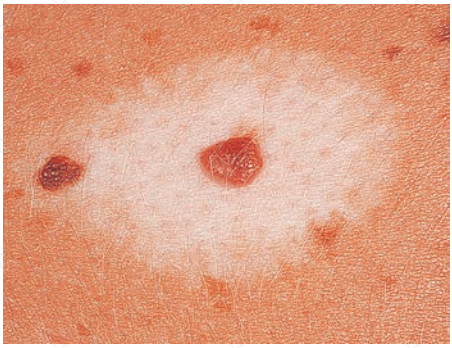

Fig. 18.10 Halo nevi are associated with vitiligo. If the nevus is atypical, it should be biopsied.

Fig. 18.12 A dermal nevus with horn pearls on the surface. It is stuck onto the surface and has the consistency of a seborrheic keratosis.

Fig. 18.11 Recurrent nevi may look clinically and histologically like melanoma.

Fig. 18.13 A dome-shaped smooth-surfaced papule. This common presentation for a dermal nevus occurs on the face and trunk. Patients are often more concerned with elevated lesions than with flat, dark lesions.

Course and Prognosis

- Acquired melanocytic nevi arise during childhood until about age 30 years and then slowly regress over a number of years.

Differential Diagnosis

- Atypical (dysplastic) nevus
- Melanoma
- Hemangioma
- Pyogenic granuloma
- Juvenile xanthogranuloma

Treatment

- Acquired melanocytic nevi do not require treatment.
- Sun precautions (sunscreen and sun-protective clothing) prevent the occurrence of acquired melanocytic nevi.
- Pigmented nevi that are irritated may be removed, although irritation does not induce malignant transformation.

Pearls

- Acquired melanocytic nevi on skin areas with limited sun exposure and newly acquired nevi after age 30 years should be regarded as suspicious.
- Spitz nevi in adults should be closely evaluated for melanoma because both are similar histologically.
- Adults with halo nevi should have a full skin examination to look for an occult melanoma.
- A new "junctional melanocytic nevus" in an adult is suspicious for early melanoma.

Fig. 18.14 Speckled lentiginous nevi are common benign hairless brown lesions, dotted with darker brown to black specks.

Fig. 18.15 A common presentation for a dermal nevus on the face. The dome-shaped papule has telangiectasias on the surface and resembles a basal cell carcinoma. The lesion has remained stable for years.

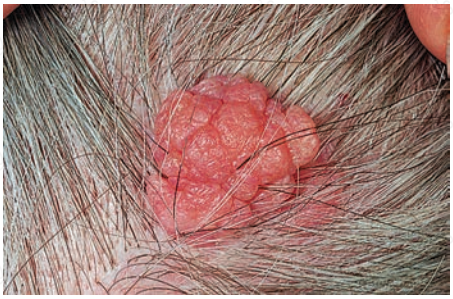

Fig. 18.16 This is a common presentation for scalp nevi. There is no pigment, and the surface is lobulated.

Fig. 18.17 A dermal nevus with no pigment. Patients commonly think that all moles are pigmented. This smooth white papule had remained unchanged for years.

Fig. 18.18 This dermal nevus has the consistency of a wrinkled sack. Biopsy showed an abundance of connective tissue and very few nevus cells.

Atypical Melanocytic Nevus (Dysplastic Nevus)

Description

- An atypical melanocytic nevus is a benign melanocytic nevus with abnormal clinical and histologic features.

History

- Approximately 10% of the U.S. population has atypical melanocytic nevi.
- Patients with multiple atypical nevi are at increased risk for melanoma, especially if there is a family history of atypical nevi and melanoma (also known as the familial atypical mole and melanoma syndrome).
- Atypical melanocytic nevi may arise at any age and continue up until the sixth decade of life.

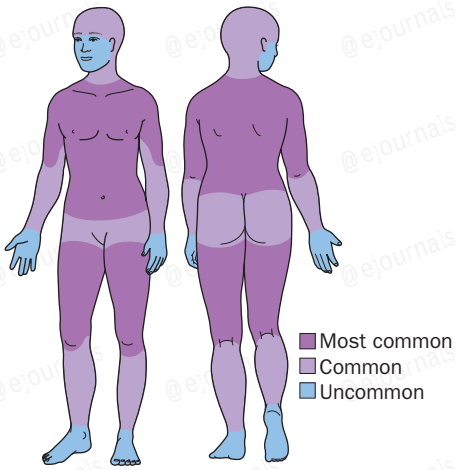

Fig. 18.19 Atypical mole syndrome distribution diagram.

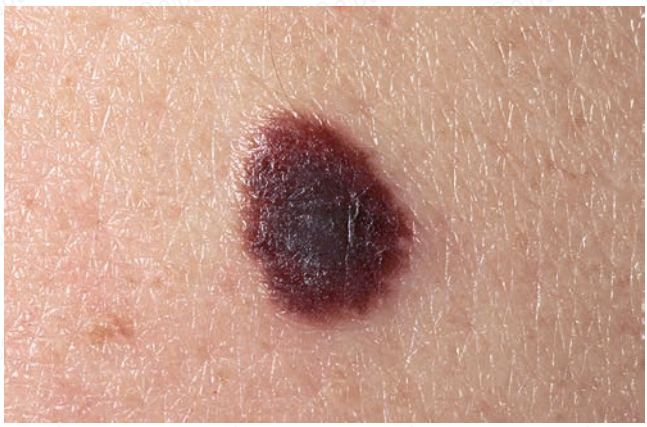

Fig. 18.20 Melanocytic nevi: junction nevus. The lesion is slightly raised, dark, and uniform.

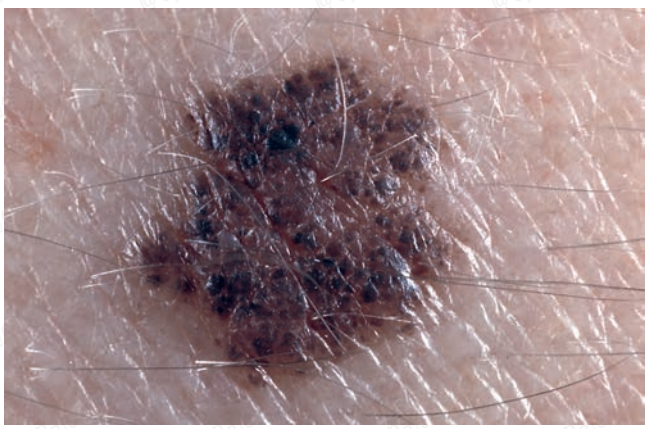

Fig. 18.21 Melanocytic nevi: compound nevus. The surface is covered with uniform brown-black dots.

Fig. 18.22 Melanocytic nevi: dermal nevus. The nevus is skin-colored colored with surface vessels and resembles basal cell carcinoma.

Fig. 18.23 Melanocytic nevi: dermal nevus. The nevus is dome shaped.

Fig. 18.24 Melanocytic nevi: dermal nevus. The nevus is skin-colored and dome shaped.

Fig. 18.25 Melanocytic nevi: dermal nevus. The nevus has a warty (verrucous) surface.

Fig. 18.26 Melanocytic nevi: dermal nevus. The nevus is polypoid.

Fig. 18.27 Melanocytic nevi: dermal nevus. The nevus is pedunculated with a soft, flabby, wrinkled surface.

Skin Findings

- Atypical melanocytic nevi show asymmetry, border irregularity, color variation, and larger size (between 6 and 15 mm in diameter).
- Atypical melanocytic nevi can appear anywhere in the skin but occur most commonly on the trunk and upper extremities.
- Patients with familial atypical mole and melanoma syndrome have atypical melanocytic nevi in sun-protected areas, such as the scalp, groin, buttocks, genitalia, breasts (in women), and the palms and soles.

Nonskin Findings

- Many atypical melanocytic nevi may indicate an increased risk for ocular melanoma.
- Eruptive atypical melanocytic nevi have been described in patients with immunosuppression, chronic myelocytic leukemia, and HIV.

Laboratory

- Histologic evaluation of an atypical melanocytic nevus is difficult and should be performed by a dermatopathologist.
- Patients with eruptive atypical melanocytic nevi should be evaluated for HIV and leukemia.

Differential Diagnosis

- Benign melanocytic nevus
- Solar lentigo
- Pigmented actinic keratosis
- Seborrheic keratosis
- Pigmented basal cell carcinoma
- Pigmented squamous cell carcinoma

Course and Prognosis

- The likelihood of an individual atypical melanocytic nevus transforming into melanoma is unknown.
- Multiple atypical melanocytic nevi are an independent risk factor for melanoma.

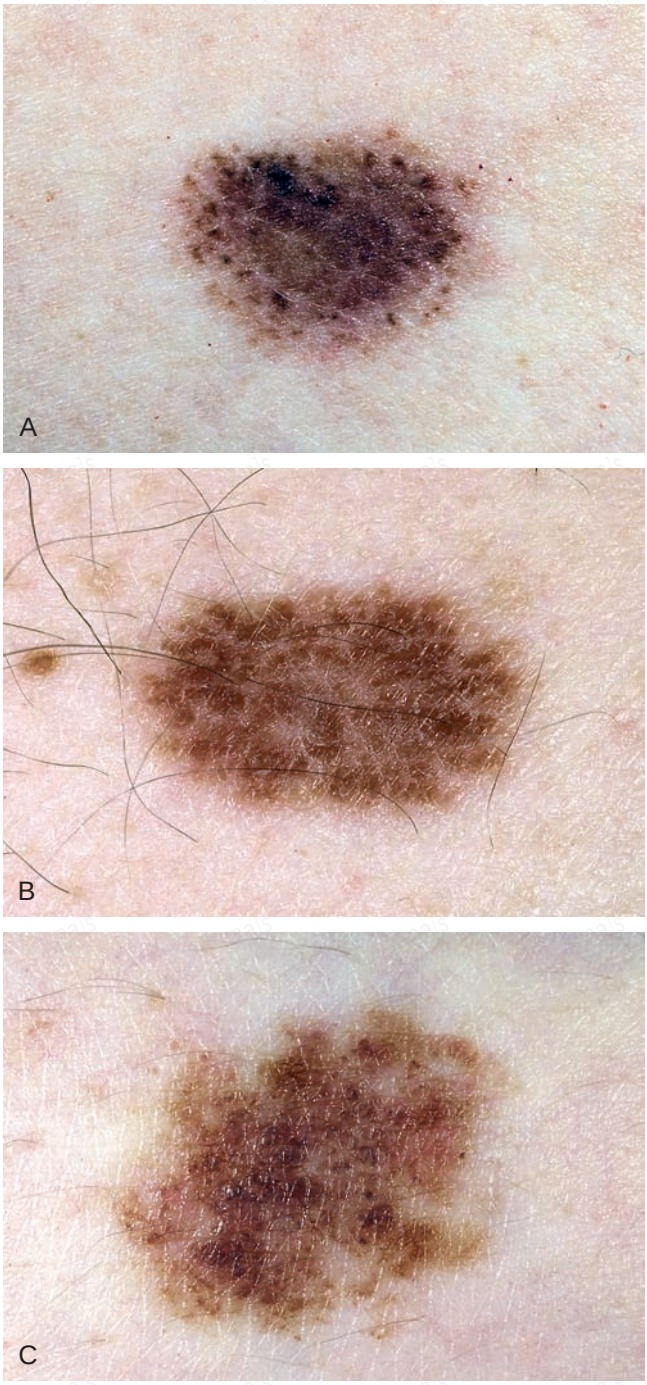

Fig. 18.28 Atypical nevi. **A,** Macular brown pigmentation with uniform dots. **B,** Brown pigmentation with a complex pattern. **C,** Clinical differentiation from melanoma is difficult.

Continued

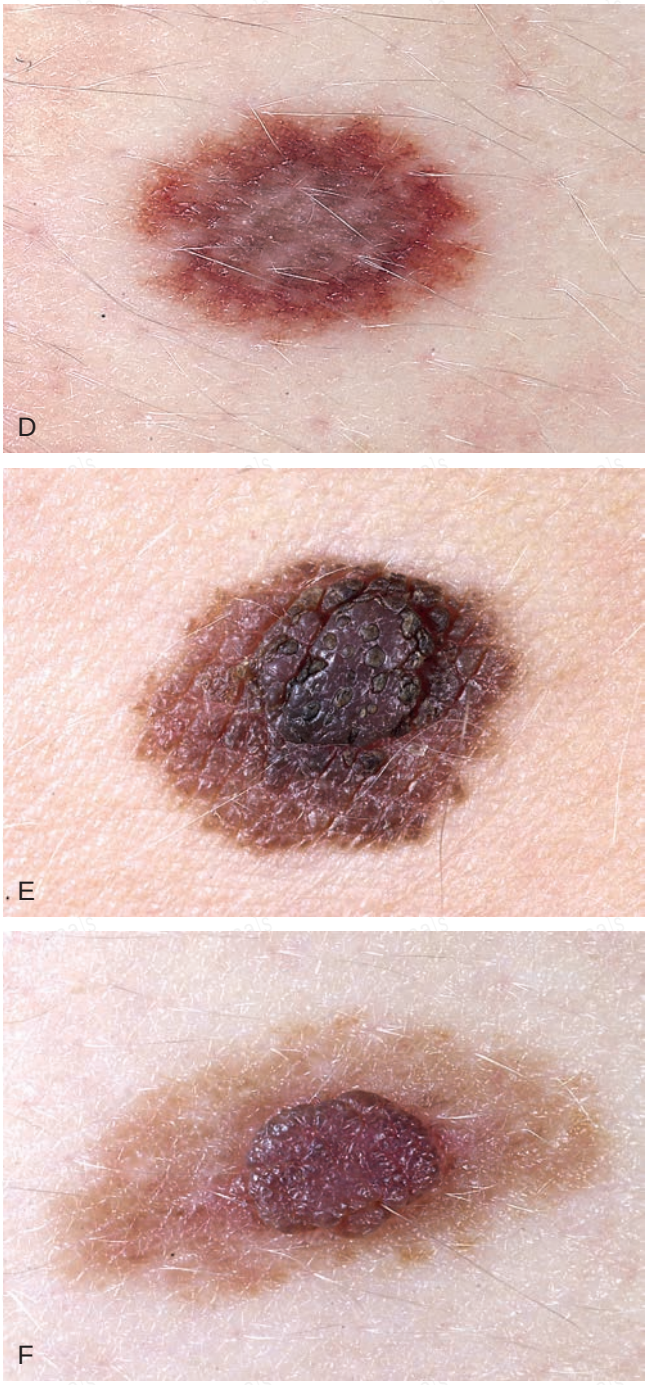

Fig. 18.28, continued D, Uniform, brown homogeneous pigmentation. **E,** "Fried-egg lesion." The papular component is dark and uniformly pigmented. **F,** "Fried-egg lesion." The macular and papular components are uniformly pigmented.

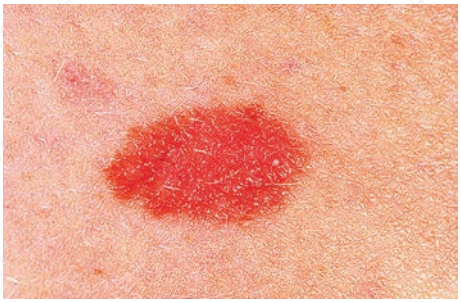

Fig. 18.29 Atypical nevi have variations in pigmentation with both papular and macular components. Differentiating them from melanoma can be difficult.

Fig. 18.30 The "fried-egg" pattern for an atypical nevus. The center is dark and raised. The macular periphery has pigmentation that fades into the surrounding skin.

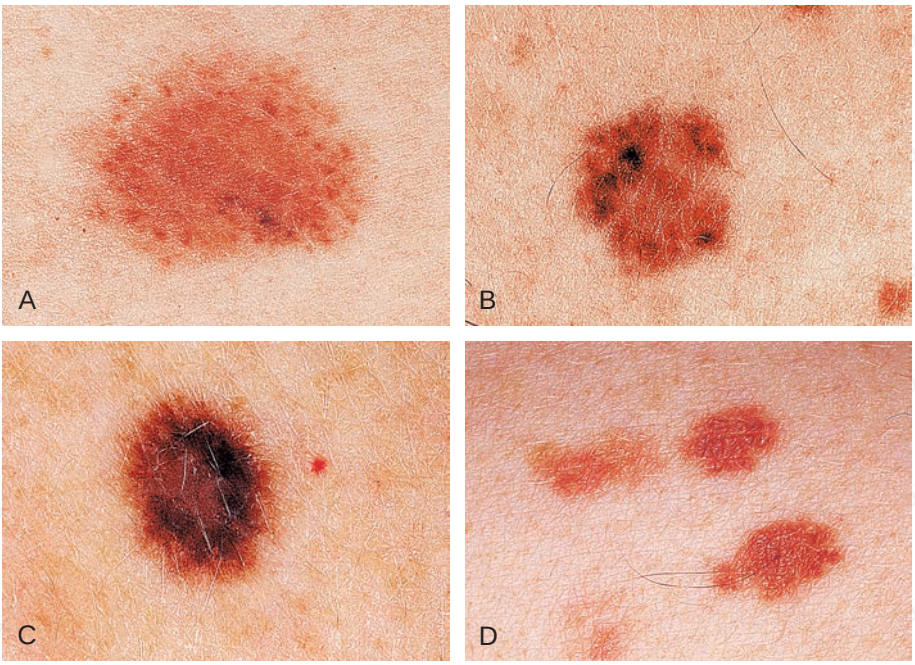

Fig. 18.31 A–D, These moles are larger than banal-appearing moles. They have a mixture of colors, including tan, brown, pink, and black. The border is irregular and indistinct and often fades into the surrounding skin. The surface is complex and variable, with both macular and papular components. A characteristic presentation is a pigmented papule surrounded by a macular collar of pigmentation ("fried-egg" lesion).

- Patients with at least five atypical melanocytic nevi are at increased risk for melanoma.
- There is 32-fold increase risk for melanoma if a patient has multiple atypical melanocytic nevi, outside the setting of familial atypical mole and melanoma syndrome.
- Patients with familial atypical mole and melanoma syndrome have a relative risk of up to 500-fold for developing melanoma.

Treatment

- Patients with atypical melanocytic nevi should have routine skin examinations, beginning around puberty.
- Atypical melanocytic nevi should be completely removed when biopsied. Partial biopsies do not allow for adequate histological examination.
- Follow-up skin examinations are usually performed every 3 to 12 months, depending on the risk for melanoma (e.g., familial atypical mole and melanoma syndrome patients are followed every 3 months).
- Skin examination should not be limited to sun-exposed areas and should include careful inspection of the scalp, genitalia, and acral regions.
- A baseline ophthalmologic examination should be obtained because patients may also be at increased risk for intraocular melanoma.
- First-degree relatives should have a baseline skin examination.
- Photography can be extremely useful in identifying changes in melanocytic nevi.
- Patients should perform monthly to quarterly self-examinations.
- Sun avoidance and sun-protective clothing are recommended.

Pearls

- Prophylactic removal of nonworrisome atypical melanocytic nevi does not decrease melanoma risk. Patients often will want "all of their nevi removed."
- Follow patients closely with photography and only biopsy changing or clinically worrisome atypical melanocytic nevi.

Melanoma

Description

- Melanoma is a malignancy arising from melanocytes.

History

- The skin is the most common site affected by melanoma.
- Melanoma arises on mucosal surfaces, the eye, and the leptomeninges.
- There are more than 76,000 new cases detected per year and more than 10,000 deaths attributed to melanoma in the United States.
- The rate of melanoma is rising at a rate of 1.4% each year in the United States.
- Survival improves with early melanoma detection.
- Thirty percent of melanomas develop within a pre-existing nevus, whereas the remaining 70% develop de novo.

Skin Findings

- When melanoma develops in a pre-existing melanocytic nevus, there is usually a focal area of color change.
- Focal color change is more specific for melanoma than the color itself (e.g., no one color is diagnostic).
- Slate-gray, black, or deep blue color indicates melanin pigment deep within the dermis.
- Pink or red indicates inflammation.
- White indicates regression or scarring.

Major Subtypes of Melanoma

- Four major clinical subtypes of melanoma are recognized, defined by clinical appearance, progression, anatomic site, and histologic appearance.

Superficial Spreading Melanoma

- Superficial spreading melanoma is the most common subtype, accounting for 70% to 80% of all melanoma.
- Most melanomas arising in a pre-existing nevus are superficial spreading melanomas.
- Superficial spreading melanoma is more common in whites, in females, and on the trunk and extremities.
- Superficial spreading melanoma tends to be larger than 6 mm and spreads laterally over a period of years before acquiring surface nodules.

Nodular Melanoma

- Nodular melanoma accounts for 15% to 30% of all melanoma.
- Nodular melanoma arises as a blue-black or pink to red nodule with scale and ulceration.
- The trunk, head, and neck are more commonly affected.
- Most nodular melanoma arises quickly over a period of several weeks to months.
- Nodular melanoma grows vertically, with no horizontal growth phase.

Lentigo Maligna Melanoma

- Lentigo maligna melanoma arises within a precursor lesion called *lentigo maligna* (melanoma in situ) and accounts for 5% to 10% of all melanoma.
- Five percent of lentigo maligna progresses to lentigo maligna melanoma.
- Lentigo maligna melanoma slowly grows over a period of years on sun-damaged skin and is more common during the seventh decade of life.
- Lentigo maligna melanoma is brown with irregular edges and pigmentation.

Table 18.1 The ABCDs of Malignant Melanoma Recognition

A	Asymmetry	One half of the lesion does not look like the remaining half.
B	Border irregularity	The border is scalloped or has focal "pseudopod" extension into the surrounding skin.
C	Color variegation	Lesions can have varying hues and varying colors.
D	Diameter >6 mm	The longest axis of the lesion is measured.

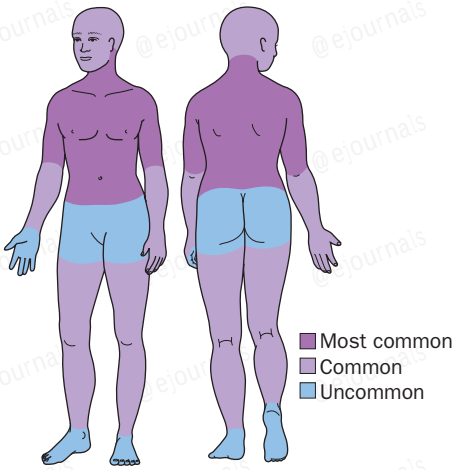

Fig. 18.32 Malignant melanoma, lentigo maligna distribution diagram.

- Dermoscopic examination shows hyperpigmented follicular openings ("circle in a circle").
- Wood's lamp shows pigmentation beyond what can be seen with ambient white light.

Acral Lentiginous Melanoma

- Acral lentiginous melanoma accounts for 5% of all melanoma and is the most common type of melanoma in Asians and blacks.
- Acral lentiginous melanoma occurs on the palms and soles and around the nail unit.
- Acral lentiginous melanoma is a slowly expanding brown to black macule with irregular borders and color variation.
- Often, acral lentiginous melanoma evolves over a period of years.

Other Melanoma Subtypes

Amelanotic Melanoma

- *Amelanotic melanoma* is a descriptive term for a nonpigmented melanoma; any subtype can be amelanotic.
- Two percent of all melanomas are amelanotic.
- Amelanotic melanoma may appear as a nonspecific lesion, such as an arthropod bite.
- At least one third of melanomas occurring on the mucosal surfaces are amelanotic.

Desmoplastic Melanoma

- Desmoplastic melanoma can occur de novo or as part of lentigo maligna, acral lentiginous melanoma, and mucosal melanoma.
- Desmoplastic melanoma is more common on sun-exposed skin and may be a skin-colored, brown, or black plaque.

Nonskin Findings

- Lymphadenopathy may indicate distant spread of melanoma.

Laboratory

- Skin biopsy is necessary to confirm melanoma diagnosis.
- Sentinel lymph node biopsy is performed for lesions greater that 1 mm in thickness.

Differential Diagnosis

Superficial Spreading Melanoma

- Acquired melanocytic nevus
- Atypical melanocytic nevus

Nodular Melanoma

- Pigmented basal cell carcinoma
- Angiokeratoma
- Hemangioma
- Traumatized nevus or acrochordon
- Pyogenic granuloma
- Lentigo maligna
- Spreading pigmented actinic keratosis
- Bowen's disease
- Solar lentigo

Lentigo Maligna Melanoma

- Lentigo
- Seborrheic keratosis
- Squamous cell carcinoma

Acral Lentiginous Melanoma

- Seborrheic keratoses
- Solar lentigo

Course and Prognosis

- The thinner the melanoma, the better the prognosis.
- Female patients and younger patients tend to have a more favorable prognosis.

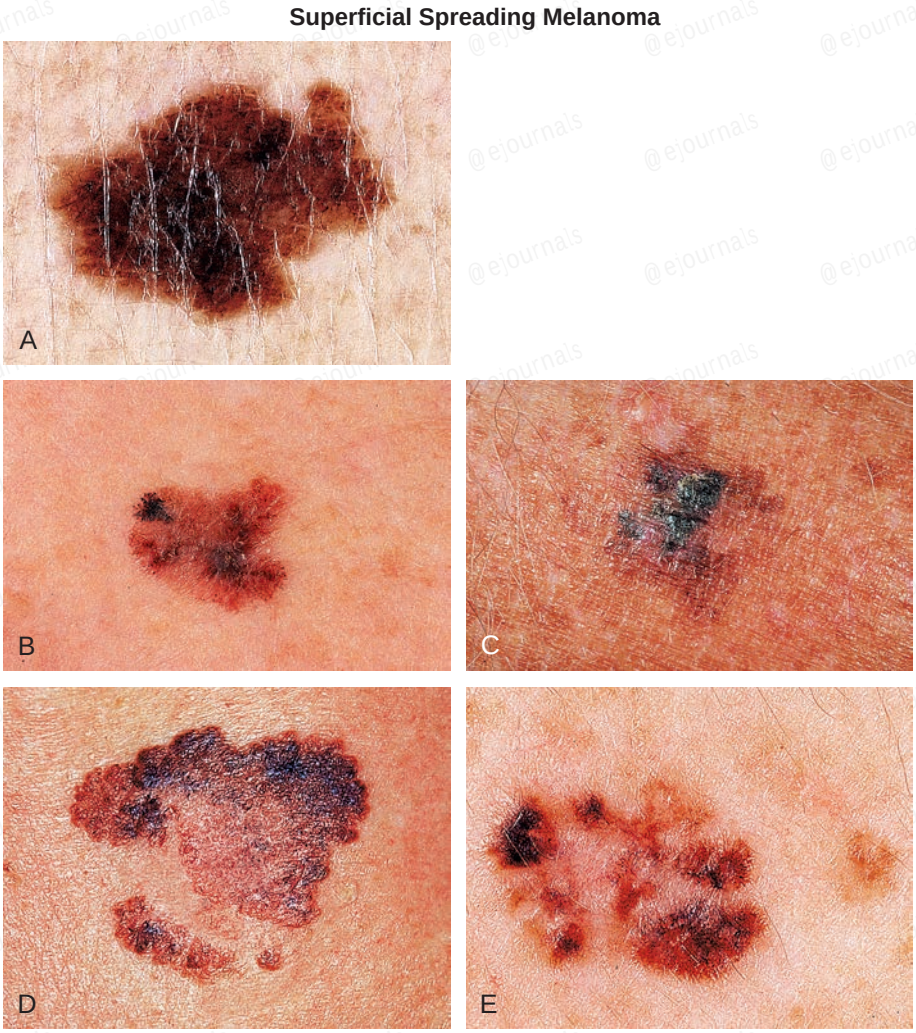

Fig. 18.33 A–E, Superficial spreading melanoma.

- A melanoma on an extremity has a more favorable prognosis than a melanoma on the trunk, head, or neck.
- Melanoma on the scalp has a worse prognosis than melanoma elsewhere on the head or neck.
- Prepubertal children have a better prognosis than adults for nodular melanoma.

Treatment

- Surgical treatment of melanoma
  - Melanoma in situ—0.5-cm margins.
  - Melanoma less than 1 mm—1-cm margins.
  - Melanoma 1.01 to 2 mm—1.0- to 2.0-cm margins.
  - Melanoma greater than 2 mm—2.0-cm margins.
- Melanoma with a thickness greater than 1 mm requires sentinel lymph node evaluation with possible staging evaluation. Computed tomography (CT) of the chest, abdomen, or pelvis, magnetic resonance imaging (MRI) of the brain, and positron-emission tomography (PET) may be required.
- Adjuvant therapy with interferon, chemotherapy, and immunotherapy is required for metastatic melanoma.

Nodular Melanoma

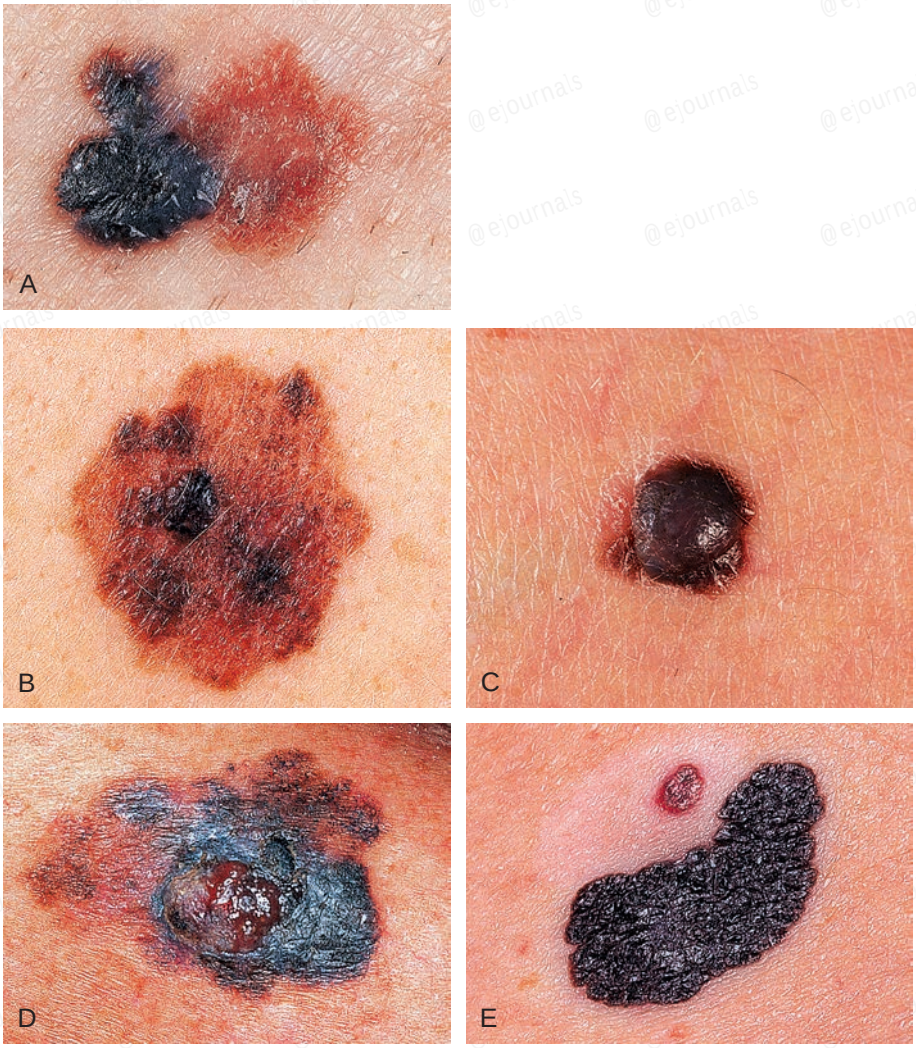

Fig. 18.34 A–E, Nodular melanoma.

Pearls

- Inquire about pancreatic cancer because some patients with melanoma may have a cancer syndrome.
- Follow patients closely every 3 months, especially if they have had multiple melanomas.
- Melanoma in prepubertal children is often amelanotic and looks similar to a pyogenic granuloma.

Lentigo Maligna and Lentigo Maligna Melanoma

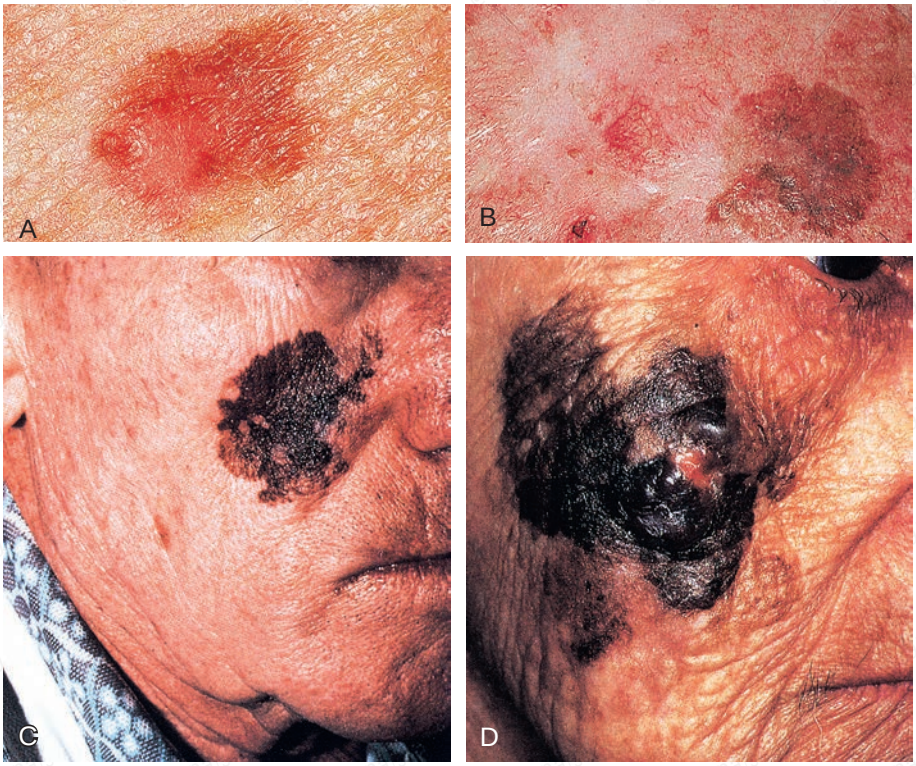

Fig. 18.35 A–D, Lentigo maligna and lentigo maligna melanoma.

Fig. 18.36 This uniformly brown macule on the ear developed a focal gray and red focus after many years. Excision confirmed lentigo maligna.

Table 18.2 Survival Rates

Stage	Disease Characteristics	Five-Year Survival Rate (%)	Ten-Year Survival Rate (%)
IA	Breslow <1.0 mm, Clark II/III, without ulceration	97	95
IB	Breslow <1.0 mm, Clark IV/V, with ulceration Breslow 1.01–2.0 mm without ulceration	92	86
IIA	Breslow 1.01–2.0 mm with ulceration Breslow 2.01–4.0 mm without ulceration	81	67
IIB	Breslow 2.01–4.0 mm with ulceration Breslow >4.0 mm without ulceration	70	57
IIC	Breslow >4.0 mm with ulceration	53	40
IIIA	Tumor any thickness without ulceration and one to three positive lymph nodes with micrometastases	78	68
IIIB	Tumor any thickness with ulceration and one to three positive lymph nodes with micrometastases Tumor any thickness without ulceration and one to three positive lymph nodes with macrometastases Tumor any thickness with ulceration and in-transit metastases or satellites without involved regional lymph nodes	59	43
IIIC	Tumor any thickness with ulceration and one to three positive lymph nodes with macrometastases Tumor any thickness and four or more involved regional lymph nodes, or matted nodes, or in-transit metastases or satellites with involved regional lymph nodes	40	24
IV	Presence of distant metastases regardless of tumor thickness or status of regional lymph nodes	15–20	10–15

Acral Lentiginous Melanoma

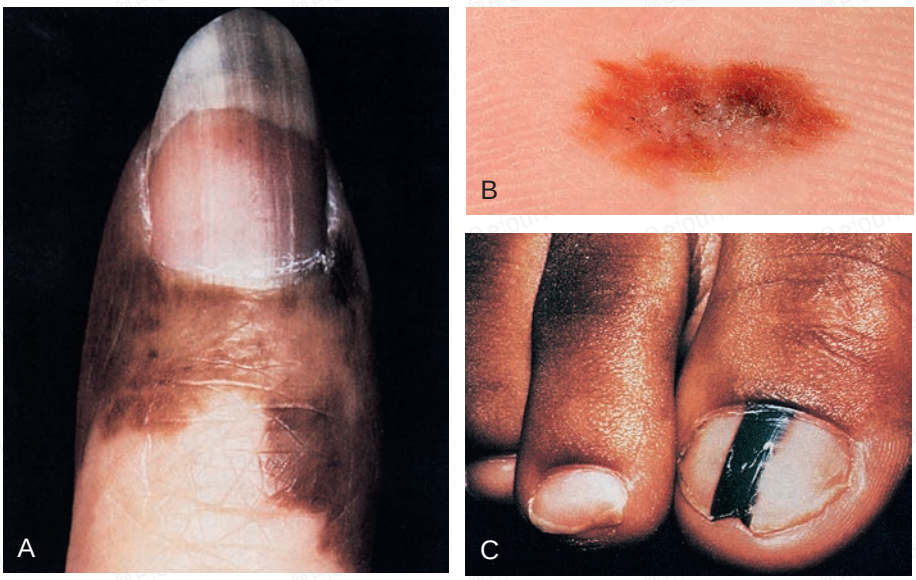

Fig. 18.37 A–C, Acral lentiginous melanoma.

Fig. 18.38 Melanoma mimics: darkly pigmented smooth-surfaced seborrheic keratosis with horn pearls imbedded in the mass.

Fig. 18.39 Melanoma mimics: inflamed seborrheic keratosis with a crusted surface and red border.

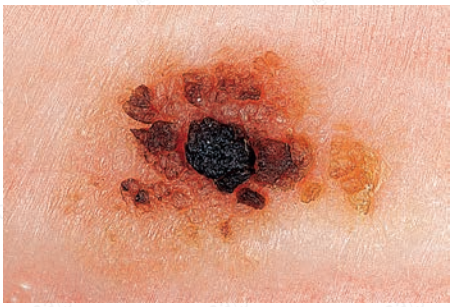

Fig. 18.40 Melanoma mimics: rough-surfaced seborrheic keratosis with an irregular border.

Fig. 18.41 Melanoma mimics: inflamed seborrheic keratosis with a crusted surface and red border.

Fig. 18.42 Melanoma mimics: darkly pigmented rough-surfaced seborrheic keratosis.

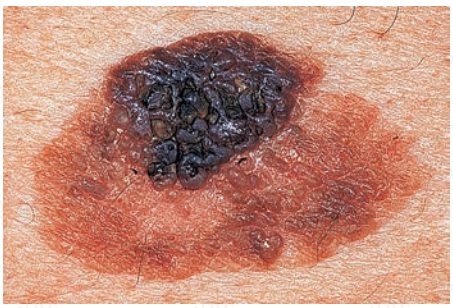

Fig. 18.43 Melanoma mimics: rough-surfaced seborrheic keratosis with an asymmetric border.

Fig. 18.44 Melanoma mimics: a pigmented basal cell carcinoma with a lobular surface and an irregular border.

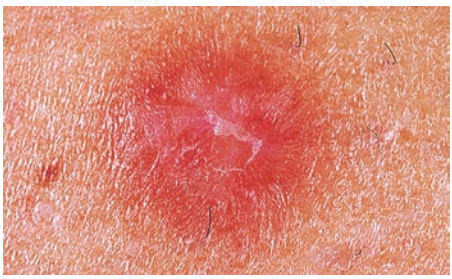

Fig. 18.46 Melanoma mimics: dermatofibroma with a brown, irregular border and central clearing.

Fig. 18.48 Melanoma mimics: a bizarre surface pattern occurred after infarction of some of the vessels in this hemangioma. The black surface papules look like nodular melanoma.

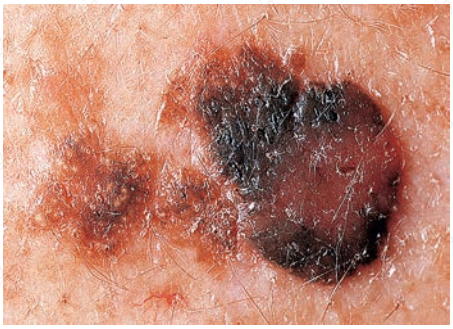

Fig. 18.45 Melanoma mimics: smooth seborrheic keratosis with variation in pigmentation and an irregular border.

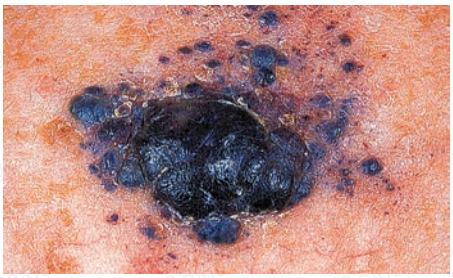

Fig. 18.47 Melanoma mimics: hemangiomas vary in size and color. This complex lesion resembles a nodular melanoma.

Fig. 18.49 Blue nevus. Blue nevi should be excised for biopsy if they are recent in onset.

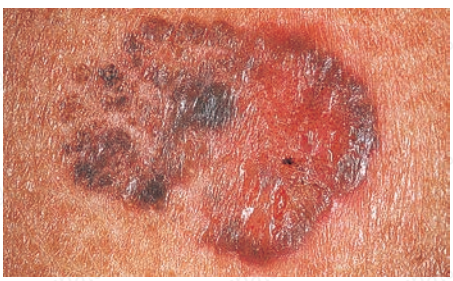

Fig. 18.50 A pigmented basal cell carcinoma with areas of regression.

Congenital Melanocytic Nevi

Description

- Congenital melanocytic nevi are melanocytic nevi that are present at birth.

History

- Congenital melanocytic nevi occur in 1% of infants.
- Congenital melanocytic nevi are sporadic and are not inherited.
- Congenital melanocytic nevi may be classified by diameter: small congenital nevi are less than 1.5 cm, medium are 1.5 to 20 cm, and large are greater than 20 cm, adjusted for final adult size.

Skin Findings

- Congenital melanocytic nevi are usually dark brown papules and plaques with an irregular verrucous surface. Most have increased terminal hairs.
- Smaller congenital melanocytic nevi associated with a large congenital nevus are referred to as *satellite nevi* and do not become malignant.
- Proliferative nodules are black nodules occurring on the surface of a large congenital melanocytic nevus and may mimic melanoma.

Nonskin Findings

- Patients with giant congenital melanocytic nevi may have associated neurocutaneous melanosis. Signs of neurocutaneous melanosis include seizures, cranial nerve palsies, sensorimotor deficits, bowel and bladder dysfunction, and developmental delay.
- Congenital melanocytic nevi may develop nonmelanocytic tumors, such as rhabdomyosarcoma and liposarcoma.

Laboratory

- MRI is considered for infants at risk for neurocutaneous melanosis.
- Skin biopsy should be performed on nodules suspicious for melanoma. Dermatopathologists should be consulted because proliferative nodules may mimic melanoma.

Course and Prognosis

- The risk for malignant melanoma increases with the size of the congenital nevus.
- Multiple satellite nevi increase the risk for melanoma.
- The greatest risk for melanoma is seen in infants with a large congenital nevus greater than 40 cm in diameter located on the trunk and with multiple satellite nevi.
- Large congenital nevi in the midline of the back have an increased risk for involvement of the brain (e.g., neurocutaneous melanosis).
- Postzygotic mutations in the *NRAS* gene are responsible for multiple congenital melanocytic nevi and neurocutaneous melanosis.

Treatment

- Small congenital melanocytic nevi can be followed, similarly to acquired melanocytic nevi.
- Medium-sized congenital melanocytic nevi should be excised before puberty if they are in location that is difficult to follow, such as the back or the scalp, or if they are atypical in appearance (e.g., asymmetric, irregular in color, irregular edges).
- Large congenital melanocytic nevi should be removed in infancy, if technically possible. MRI should be performed to evaluate for neurocutaneous melanosis. If there is central nervous system involvement, multiple surgeries may not be warranted. Patients should be referred to clinicians familiar with the management of these complex melanocytic lesions.
- Scalp melanocytic nevi are best removed in infancy when the skin is pliable, allowing for easier skin closure.

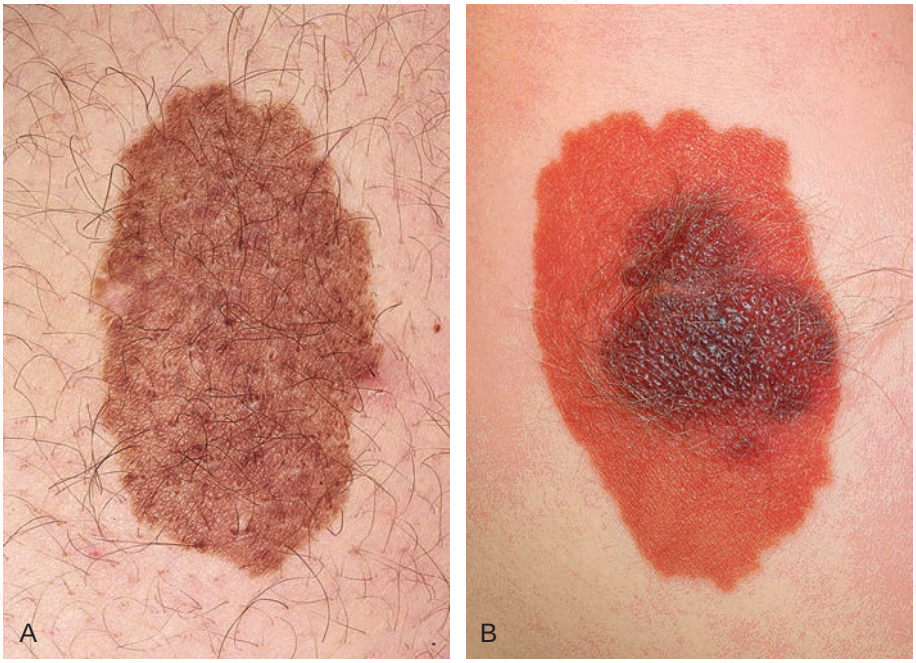

Fig. 18.51 A, B, Congenital nevi with uniform surface characteristics and light pigmentation have little chance of degenerating into melanoma. Those with dense pigmentation or irregular pigmentation like the lesion on the right are considered for excision.

Fig. 18.52 Giant congenital nevus. This infant is at risk for melanoma, and he should be sent to a multidisciplinary clinic for management.

Melanoma Staging

- The system most often used to stage melanoma is the American Joint Commission on Cancer (AJCC) TNM system. Several tests and procedures are used to assign T, N, and M categories and a grouped stage. The TNM system for staging contains three key pieces of information:
  - T stands for tumor (its size and how far it has spread within the skin). The T category is assigned a number (from 0–4) based on the tumor's thickness. It is also assigned a small letter "a" if it is not ulcerated or a "b" if it is ulcerated.
  - N stands for spread to nearby lymph nodes. The N category is assigned a number (from 0–3) based on whether the melanoma cells have spread to lymph nodes or are found in the lymphatic channels connecting the lymph nodes. It is also assigned a small letter: "a" if melanoma cells can only be seen with the microscope or "b" if they can be seen with the naked eye. A letter "c" is assigned if there are very small areas of melanoma in the nearby skin or if the melanoma is in skin lymphatic channels around the tumor (but not in the nodes themselves).
  - The M category is based on whether the melanoma has metastasized to distant organs.
- There are actually two types of staging for melanoma:
  - Clinical staging is done based on what is found on physical examination, biopsy of the melanoma, and any imaging tests that are done.
  - Pathologic staging uses all of this information, plus what is found during biopsies of lymph nodes or other organs. Therefore the clinical stage (determined before the node biopsy) may actually be lower than the pathologic stage (determined after the node biopsy).
- The T category is based on the thickness of the melanoma seen in the skin biopsy. This is an important part of determining a patient's prognosis.
- The Breslow measurement is the thickness of the melanoma under microscopy in millimeters.
- The Clark level describes how far a melanoma has penetrated into the skin.
  - The cancer stays in the epidermis (Clark level I).
  - The cancer has begun to invade the upper dermis (Clark level II).
  - The cancer involves most of the upper dermis (Clark level III).
  - The cancer has reached the lower dermis (Clark level IV).
  - The cancer has invaded to the subcutis (Clark level V).
- The Breslow measurement of thickness is generally thought to be more useful than the Clark level of penetration in determining a patient's outlook. The thickness is easier to measure and depends less on the pathologist's judgment. But sometimes the Clark level shows that a melanoma is more advanced than doctors may think it is from the Breslow measurement. The Clark level is used to stage thin melanomas (T1; see later).
- Using these systems, the possible values for T are:
  - TX: Primary tumor cannot be assessed.
  - T0: No evidence of primary tumor.
  - Tis: Melanoma in situ (Clark level I, it remains in the epidermis).
  - T1a: The melanoma is ≤1.0 mm thick, without ulceration (Clark level II or III).
  - T1b: The melanoma is ≤1.0 mm thick (Clark level IV or V) or with ulceration.
  - T2a: The melanoma is 1.01–2.0 mm thick without ulceration.
  - T2b: The melanoma is 1.01–2.0 mm thick with ulceration.
  - T3a: The melanoma is 2.01–4.0 mm thick without ulceration.
  - T3b: The melanoma is 2.01–4.0 mm thick with ulceration.
  - T4a: The melanoma is >4.0 mm without ulceration.
  - T4b: The melanoma is >4.0 mm with ulceration.

N Categories

- The possible values for N depend on whether or not a sentinel lymph node biopsy was done.

- The clinical staging of the lymph nodes is listed here; it is done without the sentinel node biopsy:
  - NX: Nearby (regional) lymph nodes cannot be assessed.
  - N0: No spread to nearby lymph nodes.
  - N1: Spread to one nearby lymph node.
  - N2: Spread to two or three nearby lymph nodes, *or* spread of melanoma to nearby skin or toward a nearby lymph node area (without reaching the lymph nodes).
  - N3: Spread to four or more lymph nodes, *or* spread to lymph nodes that are clumped together, *or* spread of melanoma to nearby skin or toward a lymph node area and into the lymph node(s).
- After a lymph node biopsy, the pathologic stage can be determined. The involvement of any lymph nodes can be subdivided as follows:
  - Any Na (N1a, N2a, etc.) means that the melanoma in the lymph node is only seen under the microscope.
  - Any Nb (N1b, N2b, etc.) means that the melanoma in the lymph node is visible to the naked eye.
  - N2c means the melanoma has spread to very small areas of nearby skin (satellite tumors) or has spread to skin lymphatic channels around the tumor without reaching the lymph nodes.

M Categories

- The M values are:
  - MX: Presence of distant metastasis cannot be assessed.
  - M0: No distant metastasis.
  - M1a: Distant metastases to skin or subcutaneous (below the skin) tissue or distant lymph nodes.
  - M1b: Metastases to lung.
  - M1c: Metastases to other organs.

Stage Grouping

Stage 0

- Tis, N0, M0: The melanoma is in situ, meaning that it involves the epidermis but has not spread to the dermis (lower layer). This is also called Clark level I.

Stage IA

- T1a, N0, M0: The melanoma is <1.0 mm in thickness and Clark level II or III. It is not ulcerated, appears to be localized in the skin, and has not been found in lymph nodes or distant organs.

Stage IB

- T1b or T2a, N0, M0: The melanoma is <1.0 mm in thickness and is ulcerated or Clark level IV or V, or it is 1.01–2.0 mm and is not ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs.

Stage IIA

- T2b or T3a, N0, M0: The melanoma is 1.01–2.0 mm in thickness and is ulcerated, or it is 2.01–4.0 mm and is not ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs.

Stage IIB

- T3b or T4a, N0, M0: The melanoma is 2.01–4.0 mm in thickness and is ulcerated, or it is >4.0 mm and is not ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs.

Stage IIC

- T4b, N0, M0: The melanoma is >4.0 mm and is ulcerated. It appears to be localized in the skin and has not been found in lymph nodes or distant organs.

Stage IIIA

- T1a–4a, N1a or N2a, M0: The melanoma is not ulcerated. It has spread to one to three lymph nodes near the affected skin area, but the nodes are not enlarged and the melanoma is found only when they are viewed under the microscope. There is no distant spread. The thickness of the melanoma is not a

factor, although it is usually thick in people with stage III melanoma.

Stage IIIB

- T1b–4b, N1a or N2a, M0: The melanoma is ulcerated. It has spread to one to three lymph nodes near the affected skin area, but the nodes are not enlarged and the melanoma is found only when they are viewed under the microscope. There is no distant spread.
- T1a–4a, N1b or N2b, M0: The melanoma is not ulcerated. It has spread to one to three lymph nodes near the affected skin area. The nodes are enlarged because of the melanoma. There is no distant spread.
- T1a/b–4a/b, N2c, M0: The melanoma can be ulcerated or not. It has spread to small areas of nearby skin or lymphatic channels around the original tumor, but the nodes do not contain melanoma. There is no distant spread.

Stage IIIC

- T1b–4b, N1b or N2b, M0: The melanoma is ulcerated. It has spread to one to three lymph nodes near the affected skin area. The nodes are enlarged because of the melanoma. There is no distant spread.
- Any T, N3, M0: The melanoma can be ulcerated or not. It has spread to four or more nearby lymph nodes, *or* to nearby lymph nodes that are clumped together, *or* it has spread to nearby skin or lymphatic channels around the original tumor and to nearby lymph nodes. The nodes are enlarged because of the melanoma. There is no distant spread.

Stage IV

- Any T, any N, M1: The melanoma has spread beyond the original area of skin and nearby lymph nodes to other organs, such as the lung, liver, or brain, or to distant areas of the skin or lymph nodes. Neither the lymph node status nor thickness is considered, but typically the melanoma is thick and has also spread to lymph nodes.

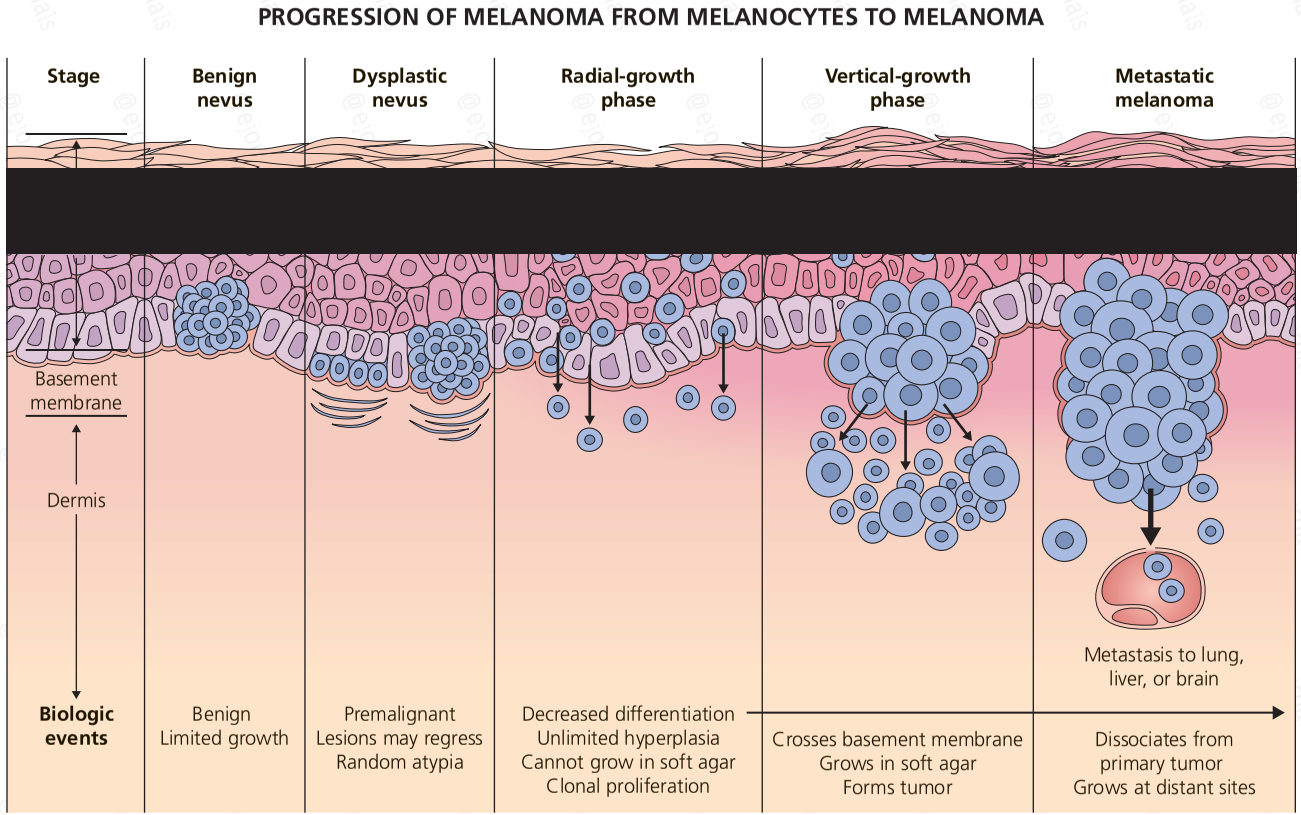

Fig. 18.53 The proliferation of melanocytes in the process of forming nevi and subsequent development of dysplasia, hyperplasia, invasion, and metastasis.

Vascular Tumors and Malformations 19

James G. H. Dinulos

Infantile Hemangiomas

Description

- Infantile hemangiomas are benign red, purple, or blue vascular neoplasms occurring within the first year of life; they consist of proliferating endothelial-like cells.
- Terms such as strawberry hemangioma and cavernous hemangioma should be discarded because they have been used to describe both vascular growths and vascular malformations.

History

- Infantile hemangiomas are the most common vascular tumor of infancy, occurring in 4% to 5% of the population.
- Infantile hemangiomas may be classified as superficial, deep, mixed (superficial and deep), localized (focal), or segmental (involving one or more embryologic segment).
- Thirty percent of infantile hemangiomas are noticeable at birth, and most are detected within the first 3 weeks of life. Deeper lesions may be noted later, but usually within the first month of life.
- They occur with increased frequency in girls and premature infants and have a predilection for the head and neck.

Skin Findings

- Onset and rate of growth, as well as depth in the skin, determine when they become noticeable.
- Nascent infantile hemangiomas (early) may appear flat and pale-white with a few telangiectasias and large dilated blood vessels.
- During the growth phase, they are seen as bright-red (superficial) or blue (deep) and feel firm and rubbery. The surface color of deeper lesions can be very subtle.
- As infantile hemangiomas begin to involute, they become slate-gray and begin to soften.
- A small percentage of infantile hemangiomas ulcerate and bleed. Ulcerations are painful and can lead to infection.
- Infantile hemangiomas appear at any anatomic site, including the oral and genital mucosa.
- Most infants have a single lesion; 15% to 20% have multiple hemangiomas.
- Multiple cutaneous hemangiomas may be associated with visceral hemangiomas (diffuse neonatal hemangiomatosis); however, infants can have visceral involvement without cutaneous involvement.

Nonskin Findings

- Infantile hemangiomas near the eyes, ears, and mouth can threaten the function of those organs.
- Infantile hemangiomas located near or on the mandible ("beard" distribution) can be associated with glottic hemangiomas.

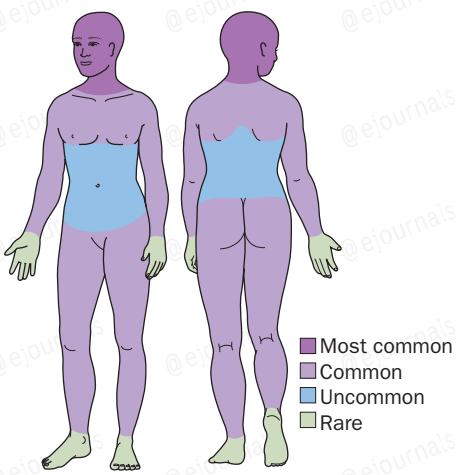

Fig. 19.1 Infantile hemangiomas distribution diagram.

Fig. 19.2 Infantile hemangiomas. Most hemangiomas are small, harmless birthmarks that proliferate for 8 to 18 months and then slowly regress over the next 5 to 8 months.

Fig. 19.3 Infantile hemangiomas. Superficial and deep hemangioma. Vital structures can be compressed, and rapidly growing areas may ulcerate.

Fig. 19.4 Infantile hemangiomas. This hemangioma is undergoing spontaneous involution.

- Infantile hemangiomas that are located in the midline can be associated with underlying cranial or vertebral anomalies.
- Large segmental facial infantile hemangiomas can be associated with malformations of other organs (PHACES syndrome is a constellation of posterior fossa malformations, hemangioma, arterial anomalies, coarctation of the aorta and cardiac defects, eye anomalies, and sternal defects).
- Large perineal hemangiomas can be associated with underlying malformations in the genitourinary tract.

Laboratory and Pathology

- Skin biopsy is not usually required to make the diagnosis of infantile hemangiomas.
- Skin biopsy can be helpful for more difficult lesions.
- At a microscopic level, proliferating lesions show well-defined masses of plump endothelial cells and pericytes forming small lumens with red blood cells; regressing lesions show flattened endothelial cells in a connective tissue stroma.
- Infantile hemangiomas express glucose transporter-1, which is thought to be a specific marker for infantile hemangiomas.
- An imaging study (an ultrasound or magnetic resonance imaging) should be done in infants with midline lumbar and

segmental facial hemangiomas because they can be associated with a tethered spinal cord and Dandy–Walker malformation, respectively. Magnetic resonance imaging of the pelvis should be obtained in patients with large perineal hemangiomas.
- Infants with multiple hemangiomas and physical signs of visceral involvement (hepatosplenomegaly, pallor, tachycardia) should have a complete blood count including platelets, abdominal ultrasound, and/or computed tomography scan.

Differential Diagnosis

- Vascular growths (pyogenic granuloma and cherry angioma)
- Rare tumors of infancy (fibrosarcoma, tufted angioma)
- Vascular malformations
- Certain types of congenital hemangiomas do not stain with glucose transporter-1

Course and Prognosis

- Infantile hemangiomas undergo proliferative, quiescent, and involutional phases.
- The most rapid growth of an infantile hemangioma is from 5.5 to 7.5 weeks of age.
- Eighty percent of infantile hemangiomas reach their maximal growth by 3 months of age.
- Most infantile hemangiomas end the proliferative phase by 9 months.
- Deep, mixed, and segmental hemangiomas may have a prolonged proliferative phase.
- Deep hemangiomas tend to have a delayed onset of growth and may proliferate for 1 month longer than superficial hemangiomas.
- Involution ends at a median age of 3 years.
- A lesion that does not show signs of regression by age 6 years is unlikely to resolve completely.
- Ulceration occurs in 15% to 25% of lesions and produces recurrent bleeding and pain.
- Superficial infection can occur but is rarely a serious problem.
- After involution, the overlying skin may appear normal, but in some instances there is some degree of atrophy or residual fibrosis.

Treatment

- Most hemangiomas of infancy should be followed closely to ensure that they are following a benign course and to reassure the parents ("active nonintervention").
- Hemangiomas of infancy should be actively treated if they are life-threatening, or if they may compromise vital functions or have potential to create permanent disfigurement (nasal tip hemangiomas). Procedures that cause scarring should be avoided, when possible.
- For ulcerations, local measures should be used in combination to remove necrotic tissue, to keep the wound moist and prevent infection.
- The wound should be gently cleansed with mild soap and a soft cloth.
- A thin layer of a topical antibiotic, such as Mupirocin 2% ointment (Bactroban), metronidazole gel (MetroGel), or bacitracin ointment, should be applied.
- The wound should be covered with an air-permeable, barrier dressing, such as polyurethane film dressing, Tegaderm, and OpSite.
- Barrier creams, such as zinc oxide 20% ointment, Desitin ointment, and A&D ointment, can be used for the perineum and other sites not amenable to topical dressings.
- Pulsed-dye laser has been used successfully for ulcerations, but in a small percentage ulcerations may actually worsen.
- Propranolol 2 to 3 mg/kg/day may be used to treat complicated hemangiomas.
- Other medical therapies include oral, intralesional and topical corticosteroids and topical timolol.
- Embolization, surgical resection, and radiation are sometimes used for complicated hemangiomas.

When to Refer

- Treatment of complicated lesions should be done in consultation with specialists. Some centers have multidisciplinary clinics staffed by dermatologists, pediatric surgeons, oncologists, and radiologists who specialize in hemangioma management.

Pearls

- Photographic documentation is helpful to follow the course of infantile hemangiomas and is reassuring to parents.
- Early referral to a specialist is essential for all complicated infantile hemangiomas.

Fig. 19.5 Infantile hemangiomas. Deeper lesions are skin-colored, red, or blue masses that are ill defined.

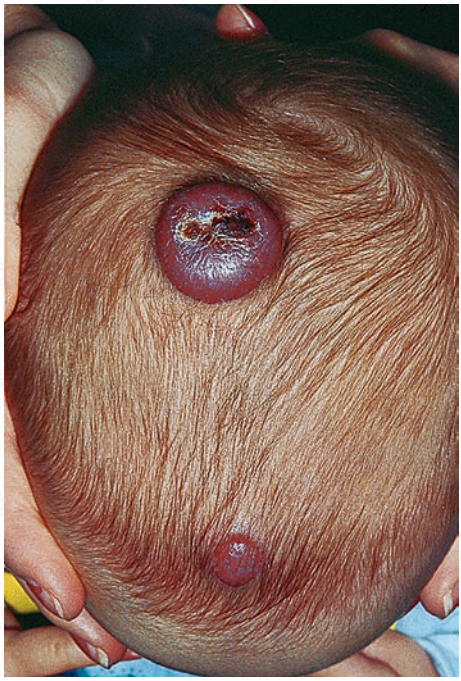

Fig. 19.6 Infantile hemangiomas. This lesion is growing rapidly. The surface is ulcerated and crusted.

Fig. 19.7 Infantile hemangiomas. A very large, deep hemangioma involving the breast. This hemangioma should be treated with oral propranolol to ensure normal breast development.

Fig. 19.8 Infantile hemangioma. Infantile hemangiomas that interfere with vital functions, such as vision, hearing, breathing, or eating, should be treated. This patient was treated with oral propranolol.

Fig. 19.9 Hemangioma. This large hemangioma on the arm has normal skin showing in the middle of the hemangioma, which is an indicator of regression.

Vascular Malformations

Description

- Vascular malformations are anomalies of blood and lymphatic vessels due to abnormal development and morphogenesis. Unlike hemangiomas, they exhibit normal endothelial cell turnover.

History

- By definition, cutaneous vascular malformations are present at birth, but they may not become noticeable for months, sometimes years.
- Vascular malformations are classified by vessel type (capillary, venous, arterial, lymphatic, mixed [common], and arteriovenous) and flow characteristics (slow flow and fast flow).
- Most vascular malformations grow in proportion to the patient.
- Most vascular malformations are sporadic and not inherited. Venous malformations can be inherited, such as multiple glomuvenous malformation and blue rubber bleb nevus syndrome (both are autosomal dominant).

Skin Findings

Capillary Malformations (Slow Flow)

- Macular staining occurs commonly on the eyelids ("angel kiss"), forehead, and nuchal area ("stork bite"). These stains tend to resolve in early childhood; however, nuchal stains commonly persist into adulthood.
- Capillary malformations can be more substantial and involve a segment and/or segments of skin innervated by the trigeminal nerve (V1–V3).

Venous Malformations (Slow Flow)

- Venous malformations usually are blue and spongy appearing; they tend to enlarge with Valsalva maneuver and can be painful.
- Phleboliths (small calcified nodules) commonly form and are felt as hard nodules.

Lymphatic Malformation (Slow Flow)

- Lymphatic malformations are composed of small channels (microcystic) or large

Fig. 19.10 Capillary malformation appear at birth as flat, irregular, red to purple patches. Later, they may become papular, simulating a cobblestone surface.

Fig. 19.11 Capillary malformation covers much of the lower extremity.

Fig. 19.12 Capillary malformation. These common capillary malformations last a life-time and are referred to as stork-bites. They may develop eczema.

Fig. 19.13 Capillary malformation. Port-wine stain. Port-wine stains develop nodules and papules with age.

channels (macrocystic) and can be localized or diffuse.
- Lymphangioma circumscripta is a microcystic lymphatic malformation consisting of small (1–5 mm) discrete, clear to blood-tinged papules that look like vesicles ("frog spawn").
- Cystic hygroma is a macrocystic (large lymphatic channels) lymphatic malformation that commonly occurs in the cervicofacial region.

Arterial Malformations (Fast Flow)
- Arterial malformations (aneurysm, stenosis, arteriovenous malformation) can cause minimal skin signs (pink stain), or they can produce massive swelling, ulceration, and necrosis.
- Arteriovenous malformations can be quiescent for years, only to cause disability through blood shunting in puberty.
- Arteriovenous malformations are most common in the head and neck region.

Nonskin Findings
- Ten percent of infants with large facial capillary malformations, especially involving trigeminal nerve V1 (forehead and upper eyelid) are at risk for underlying eye and central nervous system involvement; this triad is known as the Sturge–Weber syndrome.
- Sturge–Weber syndrome is caused by an activating mutation in the *GNAQ* gene, which increases cell proliferation and inhibits apoptosis, through the RAS effector pathways.
- In Sturge–Weber syndrome, patients can develop glaucoma (30%–70%), seizures (70%–80%), and overgrowth of the underlying facial bones.
- Large cervicofacial lymphatic malformations can cause airway compromise.
- Arteriovenous malformations can cause cardiac failure due to shunting; head and neck arteriovenous malformations can cause seizures and focal neurologic deficits.

Laboratory and Pathology
- Neurologically normal infants with large facial capillary malformations involving the forehead should be referred for head magnetic resonance imaging.
- Skin biopsy can be helpful to evaluate lesions that are difficult to characterize and will show the architecture and cell type of the corresponding malformation.

Differential Diagnosis
- Transient macular staining
- Deep infantile hemangiomas
- Nevus anemicus

Course and Prognosis
- Capillary malformations can darken with age and develop a cobblestone appearance.
- Extensive venous and arterial malformations can involve deeper structures, such as muscle, and can be a source of local or disseminated coagulopathy.

Fig. 19.14 Nevus anemicus is a rare congenital lesion most frequently observed on the chest or back of women. The lesion usually consists of a well-defined white macule with an irregular border, often surrounded by smaller white macules beyond the border of the major lesion. See the differential diagnosis.

- Vascular malformations may cause alterations in underlying bone and soft tissue, resulting in functional disability.
- Lymphatic malformations can be complicated by pain, swelling, intralesional bleeding, and infection.

Treatment

- Capillary malformations involving the forehead and lateral neck usually respond well to pulsed dye laser, whereas central facial, trigeminal nerve V2, and extremity lesions can be more difficult to treat.
- Coagulopathies associated with venous malformations have been treated with compression stockings, aspirin, low molecular weight heparin, hydrotherapy, massage, and physical therapy.
- Laser surgery, surgical resection, embolization, and sclerosis are used alone or in combination to treat complicated vascular malformations.

Fig. 19.15 Lymphangioma circumscriptum. These hamartomatous malformations consist of grouped translucent or hemorrhagic vesicles on a dull-red or brown base. Their appearance has been compared with a mass of frog's eggs ("frog spawn").

When to Refer

- Infants with large facial capillary malformations should be evaluated by a dermatologist, an ophthalmologist, and a neurologist.
- Treatment should be performed in a multidisciplinary setting by physicians experienced with vascular malformations.

Pediatric Considerations

- Early hemangiomas of infancy and vascular malformations appear similar at birth.
- Vascular malformations can become more pronounced at puberty.

Cherry Angioma

Description

- Cherry angioma is a distinct, benign vascular neoplasm found in nearly all people older than 30 years of age.

History

- Lesions appear gradually in adulthood and are asymptomatic.

Skin Findings

- Lesions are discrete 0.5- to 5.0-mm, smooth, dome-shaped to polypoid papules.
- Early smaller lesions are cherry-red, and deeper larger lesions are maroon.
- They mostly occur on the trunk but can be found on the head, neck, and extremities.
- The number of lesions may range from a few to hundreds.

Nonskin Findings

- Multiple eruptive cherry angiomas have been associated with bromide exposure, sulfur mustard gas, and the glycol ether solvent 2-butoxyethanol.
- The sudden appearance of such lesions may warrant a search for occult malignancy, especially for small tumors capable of hormone production (those in the pancreas, small bowel, and respiratory system).

Laboratory and Pathology

- Skin biopsy is rarely needed but demonstrates a sharply defined, benign proliferation of dilated capillaries, and postcapillary venules within the papillary dermis.
- Larger lesions show flattening of the overlying epidermis and a collarette of epithelium at the periphery.

Differential Diagnosis

- Telangiectasia
- Melanoma
- Pyogenic granuloma
- Bacillary angiomatosis

Course and Prognosis

- Undisturbed cherry angiomas persist indefinitely.
- Superficial trauma may produce bleeding.
- Isolated reports of patients with hundreds of cherry angiomas arising in association with pregnancy, and also in patients with elevated prolactin levels, suggest that hormonal factors may play a role.

Treatment

- Cherry angiomas may be ablated by electrocautery, laser surgery, cryosurgery, or simple scissor excision.
- There is a slight risk for scarring and dyspigmentation with treatment.

Pearls

- The presence of numerous lesions should not prompt a search for malignancy, although the explosive appearance of such lesions should raise concern.

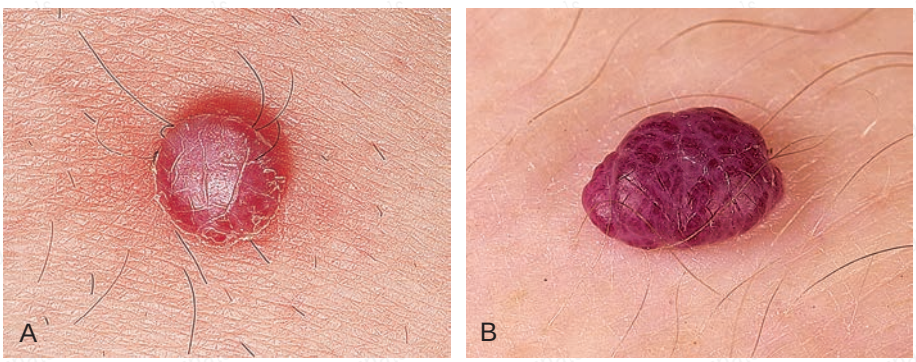

Fig. 19.16 A, B, Cherry angioma. These smooth, firm, deep-red papules of 0.5 to 5 mm occur in virtually everyone after age 30 years, and numbers increase with age.

Fig. 19.17 Cherry angiomas increase in number with age. They are frequently seen on the trunk but may occur anywhere on the skin. They present as small red macules and papules. Some people have hundreds of lesions. They are benign and can be removed for cosmetic purposes.

Angiokeratoma

Description

- Angiokeratomas are scaly papules, colored red to purple, formed by dilation of superficial blood vessels and epidermal thickening.

History

- Angiokeratomas are common and most often seen as multiple lesions restricted to specific body sites.
- There are four clinical variants determined by location and age of onset.

Angiokeratoma of Fordyce (Most Common)

- Asymptomatic multiple angiokeratomas symmetrically distributed on the scrotum and vulva.
- They appear in midlife and persist indefinitely.
- Scrotal angiokeratomas may be associated with inguinal hernia, varicosities of the leg, or varicocele; thus, increased venous pressure is thought to play a role.
- Vulvar angiokeratomas may develop at a younger age in pregnant woman or with use of oral contraceptives.

Solitary or Papular Angiokeratomas

- Solitary or papular angiokeratomas occur equally in both sexes.
- They commonly occur as a single lesion on the legs of young adults; they may be multiple and occur in any location.
- Papular angiokeratomas are larger than the other variants and easily traumatized.

Angiokeratoma of Mibelli

- Angiokeratomas of Mibelli are symmetric, grouped, multiple angiokeratomas occurring on the backs of the fingers and toes.
- They appear during childhood and adolescence and continue to increase in number.
- Because of their location, lesions may be frequently traumatized and painful.
- Lesions are more common in females and may be associated with chilblains or pernio.
- Angiokeratoma of Mibelli is inherited in an autosomal dominant manner.

Angiokeratoma Corporis Diffusum

- Fabry's disease is an X-linked recessive inborn error of metabolism caused by a deficiency of the lysosomal enzyme α-galactosidase A; this defect leads to deposition of glycophospholipids in the skin (and other organs), leading to the formation of angiokeratomas.
- Other lysosomal enzyme deficiencies (galactosidase β1-fucosidase, β-mannosidase, and neuraminidase) can produce similar symptoms to those of Fabry's disease.
- Boys are more severely affected than girls.
- Around puberty, multiple angiokeratomas form symmetrically in the bathing-trunk area.

Skin Findings

- Angiokeratoma is a deep-red to maroon, or blue to black, sharply defined papule of 0.5 to 1.0 cm.
- Early lesions are lighter in color, are soft, and are more easily compressed.
- Older lesions are darker, firmer, and more raised with surface scale.

Nonskin Findings

- Angiokeratoma corporis diffusum (Fabry's disease).
- In childhood and adolescence, boys develop episodic bouts of fever associated with severe pain in the extremities and abdomen; these crises can precede the angiokeratomas and

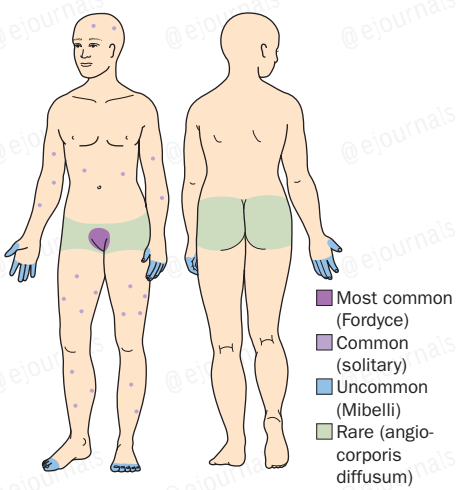

Fig. 19.18 Angiokeratoma distribution diagram.

Fig. 19.19 A, B, Angiokeratomas of Fordyce occur on the vulva and scrotum. Increased venous pressure, such as occurs with pregnancy and hemorrhoids, may be implicated.

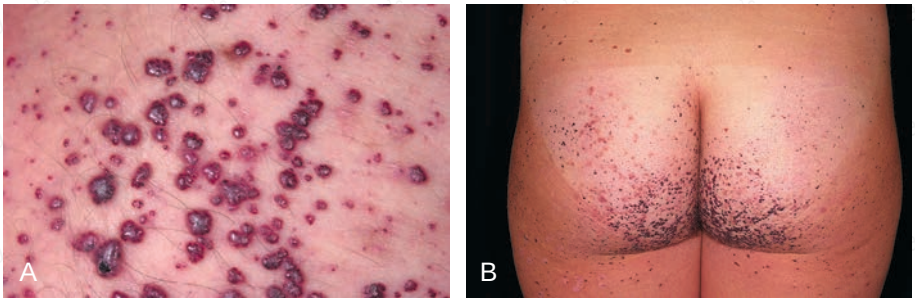

Fig. 19.20 A, B, Angiokeratoma corporis diffusum (Fabry's disease) is an X-linked disorder caused by a deficiency in alpha-galactosidase A, a lysosomal enzyme. This leads to the accumulation of glycosphingolipids in most tissues. Patients have cutaneous angiokeratomas, severe pain in the extremities, paresthesias, corneal opacities, renal failure, and many heart, gastrointestinal, and central nervous system abnormalities.

are brought on by exercise and changes in temperature.
- Girls can experience minor symptoms.
- The brain (transient ischemic attacks and stroke), heart (myocardial infarction), and kidney (renal failure) can be affected.
- Men usually die by age 50 years.
- Most males and many carrier females develop distinctive corneal opacities; this sign can be useful to detect mildly affected males and carrier females.

Laboratory and Pathology
- Skin biopsy shows dilated blood vessels in the superficial dermis with overlying hyperkeratosis.
- All angiokeratoma subtypes have similar appearances microscopically.
- Biochemical, molecular, and prenatal testing is available for Fabry's disease and other similar lysosomal storage diseases.

Differential Diagnosis
- Solitary angiokeratomas may look like malignant melanoma
- Other lesions that may resemble a solitary angiokeratoma include thrombosed common wart, Kaposi's sarcoma, pyogenic granuloma, pigmented basal cell carcinoma, and squamous cell carcinoma
- Other lysosomal storage diseases can mimic Fabry's disease

Course and Prognosis
- Undisturbed angiokeratomas persist indefinitely.
- Surface trauma often results in bleeding, but not resolution, of the lesions.

Treatment
- Cosmetically concerning lesions, or ones susceptible to trauma, can be treated with excision, electrosurgery, and laser surgery.
- Ophthalmologic and neurologic consultation should be considered in cases of angiokeratoma corporis diffusum.

When to Refer
- Children with symptoms of Fabry's disease should be referred to a dermatologist and geneticist for diagnosis, treatment, and genetics counseling.
- Patients with Fabry's disease should be seen by an eye specialist and a neurologist; other specialists, such as a cardiologist and a nephrologist, may need to be consulted.
- Women with a family history of Fabry's disease should be referred for prenatal diagnosis.

Pearls
- Patients with angiokeratomas of Fordyce should be reassured that the lesions are not sexually transmitted.

Fig. 19.21 Vomiting ecchymosis. Vomiting may cause petechia and bruising above the nipple line.

Fig. 19.22 Endometriosis. Endometriosis may mimic a hemangioma and should be considered, especially if the bleeding is cyclical.

Fig. 19.23 Hemangioma of the nose. Hemangiomas may occur in adults and are easily removed.

Venous Lake

Description

- A venous lake is a dilated vein that occurs on sun-damaged skin and appears as a small, blanchable, dark blue-to-purple papule.

History

- Venous lakes are common on the sun-exposed skin of elderly patients, especially in white men.
- Acquired sun damage and subsequent loss of dermal elasticity (solar elastosis) cause venous lakes.

Skin Findings

- A venous lake is an asymptomatic dark blue-to-purple, soft papule of 2 to 10 mm that blanches with pressure.
- Multiple lesions may be present on the mucosal surface of the lip, especially the lower lateral vermilion border.
- Lesions may also be found on the ears.
- Raised lesions and lesions subject to trauma (like the mucosal surface of the lip) can be itchy and sore, suggesting thrombosis.
- Traumatized lesions bleed easily and form a hemorrhagic crust.

Laboratory and Biopsy

- Skin biopsy shows a dilated, thin-walled venule located high in the dermis or submucosa.

Differential Diagnosis

- Venous lakes can resemble pigmented lesions such as blue nevi and malignant melanoma; venous lakes completely blanch with diascopy
- Traumatized venous lakes can become crusted and look like herpes labialis
- Patients with Kaposi's sarcoma associated with HIV can develop multiple blue-to-purple nodules on mucosal surfaces that resemble venous lakes

Course and Prognosis

- Venous lakes are persistent and may increase in size with time.

Treatment

- Reassurance of the patient is often all that is needed for venous lakes.
- Frequently traumatized or cosmetically concerning lesions and lesions that interfere with eating or speaking should be treated, although recurrence is common.
- After anesthetizing with local or regional anesthesia, the venous lake is unroofed with iris scissors and cauterized.
- Lasers are also effective for removing venous lakes.

When to Refer

- Rapidly changing lesions should be referred to a dermatologist.

Pearls

- Frequently, patients with venous lakes are concerned about malignancy.
- Venous lakes with thrombosis can be tender.
- Lesions resemble a varicosity occurring in sun-damaged skin.

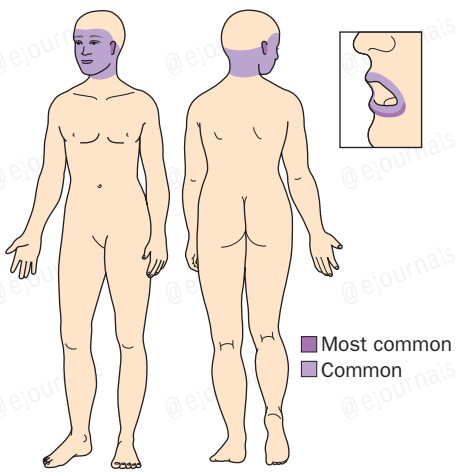

Fig. 19.24 Venous lake distribution diagram.

Pyogenic Granuloma

Description

- Pyogenic granuloma is an exophytic dome-shaped papule made up of proliferating capillaries separated by thick fibrous bands and surrounded by an epithelial collarette.
- The term pyogenic granuloma is a misnomer because it is neither infectious nor granulomatous; many pathologists use the term *lobular capillary hemangioma.*

History

- Pyogenic granulomas occur more frequently in children and young adults and are less common in elderly people.
- The cause is unknown; skin trauma and hormones are thought to be important factors because pyogenic granulomas can occur at sites of injury and during pregnancy.
- Pyogenic granuloma–like lesions can be seen in acne patients who are treated with isotretinoin.

Skin Findings

- Pyogenic granulomas are yellow to deep-red, glistening, dome-shaped to polypoid papules of 3 to 10 mm.
- Lesions grow rapidly, bleed profusely, and can be covered with yellow crust and surrounded by a collarette of scale.
- Usually, lesions do not get larger than 1 cm. They can "fall off," only to regrow.
- Gingival lesions occurring during pregnancy are referred to as *epulis gravidarum*.
- Lesions are more common on the head and neck and fingers.

Laboratory and Pathology

- A sample of the lesion should be sent for routine histology on all suspected pyogenic granulomas that are surgically treated.
- Skin biopsy shows lobules of proliferating endothelial cells, intersected by dense fibrous septi and surrounded by an epithelial collarette.
- Often the epidermis is thinned with superficial erosion and exposed capillaries; secondary inflammatory changes are common.

Differential Diagnosis

- Usually the diagnosis is straightforward, especially with single lesions
- Spitz nevi (in children)
- Amelanotic malignant melanoma, squamous cell carcinoma, basal cell carcinoma (in adults; can present as a weeping, rapidly growing nodule)
- Angiosarcoma (in elderly people, especially if it occurs on the head and neck; this malignancy also occurs in the setting of chronic lymphedema [Stewart–Treves syndrome] and after radiation therapy)
- Bacillary angiomatosis and Kaposi's sarcoma (in patients with HIV infection)

Course and Prognosis

- Pyogenic granulomas arise suddenly, attain a stable size, and persist without treatment, although some lesions spontaneously regress within 6 months.
- Larger deep-seated lesions may recur with treatment.
- Rarely, multiple satellite lesions can occur.
- Pyogenic granuloma. Bleeding exuberant pink papule is characteristic of pyogenic granuloma.

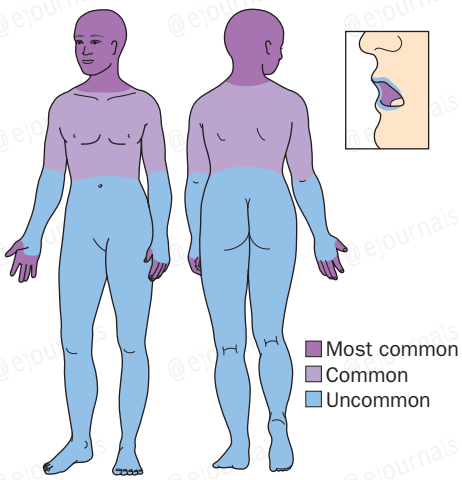

Fig. 19.25 Pyogenic granuloma distribution diagram.

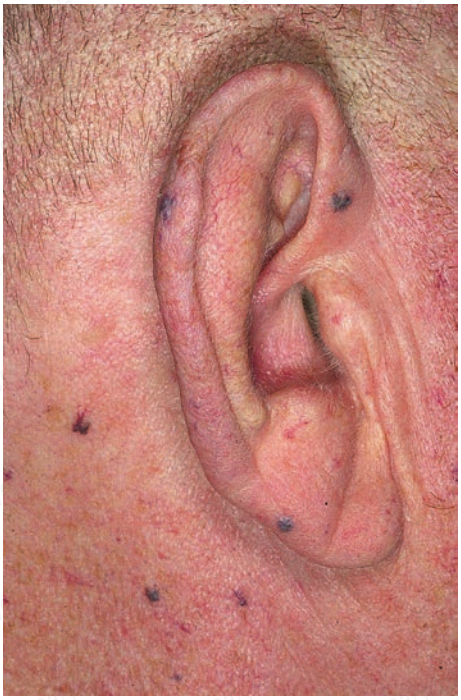

Fig. 19.26 Venous lakes occur on sun-exposed surfaces of the ears, face, neck, and lips.

Fig. 19.27 Venous lakes are dark, and patients are concerned about malignancy. The lesion should be firmly depressed to force the blood out and blanch the lesion.

Fig. 19.28 Venous lakes are common on sun-exposed surfaces of the vermilion border of the lip. Venous lakes are dark-blue, slightly elevated, 0.2- to 1-cm dome-shaped lesions composed of a dilated blood-filled vascular channel. Several lesions may occur.

Fig. 19.29 Pyogenic granuloma. A bleeding, exuberant pink papule is characteristic of pyogenic granuloma.

Fig. 19.30 Pyogenic granuloma is a small, rapidly growing, yellow to bright-red, dome-shaped fragile protrusion that has a glistening, moist to scaly surface.

Treatment

- Pyogenic granulomas are best treated by biopsy followed by electrodesiccation and curettage of the base and border of the lesion.
- Most resolve with a single crateriform scar; recurrences occur in a few patients.
- Rarely, multiple satellite lesions develop at and around the site of a previously treated pyogenic granuloma. This occurs most often on the shoulder and trunk in younger patients.

When to Refer

- Patients with recurrent or multiple pyogenic granulomas should be referred to a dermatologist for management.
- Infants and toddlers should be referred to a specialist, especially if the clinician is not experienced in diagnosing and treating young children with pyogenic granulomas.

Pearls

- Patients and parents should be advised of the possibility of recurrence after treatment.
- Children will typically have the new lesions covered with a dressing (the "band aid" sign) because of the bleeding.

Fig. 19.31 Pyogenic granuloma may bleed profusely if traumatized. The smooth dome-shaped papule with a glistening surface is highly characteristic.

Kaposi's Sarcoma

Description

- Kaposi's sarcoma is a malignancy of lymphatic endothelial cells associated with a gamma herpesvirus, human herpesvirus 8 (Kaposi's sarcoma-associated herpesvirus).
- Kaposi's sarcoma can be divided into four clinical and epidemiologic subsets: classic, endemic, immunosuppression-associated or transplant-associated, and epidemic or AIDS associated.

History

- Classic Kaposi's sarcoma is sporadic and slowly progressive and occurs predominantly in 50- to 70-year-old men of Eastern European or Mediterranean descent.
- In endemic regions (especially eastern and southern Africa), up to 50% of all childhood soft tissue tumors are due to Kaposi's sarcoma, and children can develop an aggressive lymphadenopathic form.
- People receiving immunosuppressive therapy for a variety of conditions—especially organ transplant recipients—are at risk for Kaposi's sarcoma.
- Patients of Mediterranean and Eastern European descent appear to be at increased risk for immunosuppression-associated Kaposi's sarcoma—supporting the theory of genetic predisposition.
- Epidemic-associated Kaposi's sarcoma is the most common AIDS-associated cancer and is 20 times more common in homosexual men than in those who acquired HIV by another means (e.g., through hemophilia).

Skin Findings

- The skin lesions of Kaposi's sarcoma have a variety of morphologies (macules/patches, papules/plaques, nodules), and the lesions can vary depending on the clinical variant.
- Classic Kaposi's sarcoma starts with purple patches on the distal lower extremities that progress proximally and become multifocal; individual lesions darken and thicken, eventually becoming brown and verrucous.
- Lesions on the lower legs can look eczematous and ulcerate.
- Early Kaposi's sarcoma nodules can feel soft; older nodules can feel firm.
- Endemic Kaposi's sarcoma (within Africa) involves the lymph nodes in people with localized nodular lesions. It occurs most commonly in men and children.
- Immunosuppression-associated Kaposi's sarcoma is morphologically similar to classic Kaposi's sarcoma; lesions typically improve and sometimes resolve with cessation of immunosuppressive therapy.
- Lesions in AIDS-associated Kaposi's sarcoma have a predilection for the face (especially the nose, eyelids, and ears), the torso, and oral mucosa (especially the hard palate).

Nonskin Findings

- Besides the skin, the most commonly affected organs are the lymph nodes, the gastrointestinal tract, and the lungs.
- Patients with AIDS-related Kaposi's sarcoma often have systemic involvement, particularly of the gastrointestinal tract (stomach and duodenum).
- Fever, night sweats, and weight loss may be present.

Laboratory and Biopsy

- Skin biopsy is indicated to confirm the diagnosis and shows neoplastic spindle-shaped cells that form clefts and vascular channels.
- The CD4 count in AIDS-related cases is often less than 200 cells/mL.

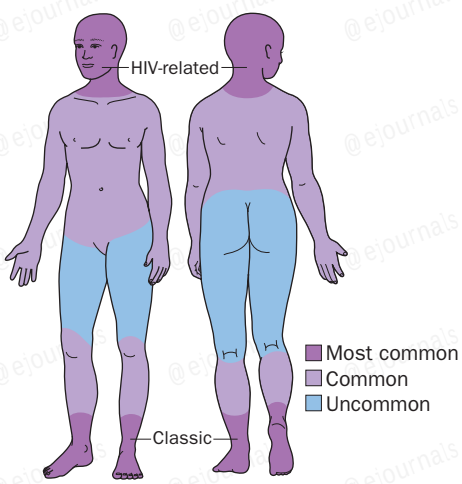

Fig. 19.32 Kaposi's sarcoma distribution diagram.

Fig. 19.33 Kaposi's sarcoma related to AIDS occurs as a multifocal and widespread disease. It begins as violaceous macules and papules and progresses to plaques with multiple red to purple nodules.

Fig. 19.34 Classic Kaposi's sarcoma begins as purple patches and plaques that involve the lower extremities.

Differential Diagnosis

- Early single lesions may look like pyogenic granuloma, malignant melanoma, or bacillary angiomatosis
- Multiple lesions may look like stasis dermatitis, progressive pigmented purpura, or cutaneous T-cell lymphoma

Treatment

Classic Kaposi's Sarcoma

- For patients with single lesions, surgical excision can be adequate.
- For multiple lesions localized to one area, radiation is the treatment of choice.
- For extensive or recurrent lesions, combination therapy with surgery, radiation, and chemotherapy often is needed.

Endemic Kaposi's Sarcoma

- Radiation and chemotherapy are used.

Immunosuppression-Associated Kaposi's Sarcoma

- Usually modification or discontinuation of the immunosuppressive therapy produces regression of Kaposi's sarcoma.
- Radiation and chemotherapy are useful for patients whose Kaposi's sarcoma does not resolve when the immunosuppressive drugs are altered.

AIDS-Associated Kaposi's Sarcoma

- Radiation therapy is very effective, especially for large, localized, and ulcerative lesions.
- Cryosurgery done in 3-week intervals improves superficial Kaposi's sarcoma and is a good cosmetic treatment.
- Intralesional vincristine has been used with success.
- Patients can be given antiretroviral therapy alone or in combination with radiation or systemic therapy, such as cytotoxic drugs and interferon-α, directed against Kaposi's sarcoma.
- Combination antiretroviral therapy has decreased the incidence of AIDS-associated Kaposi's sarcoma by 80%.

Pearls

- AIDS-associated Kaposi's sarcoma (especially facial lesions) is extremely distressing to most patients.
- Oral Kaposi's sarcoma is not uncommon in AIDS patients and may be the presenting sign of infection with HIV.

Telangiectasias

Description

- Telangiectasias are common asymptomatic dilations of capillaries, venules, and arterioles within the subpapillary plexus.

History

- Telangiectasias occur in a variety of clinical settings.
- Although there is little variation in the appearance of individual telangiectasias from one disorder to another, the age of onset, distribution, and progression vary among disorders.
- Recognition of this, along with other associated clinical findings, helps discern between the various disorders associated with telangiectasias.
- It is useful to distinguish between disorders in which telangiectasias are a primary pathologic feature and disorders in which telangiectasias arise secondarily.

Primary Telangiectasias

Hereditary Hemorrhagic Telangiectasia (Osler–Rendu–Weber Disease)

- Hereditary hemorrhagic telangiectasia is an autosomal dominant condition in which telangiectasias are found on the mucosae, skin, and internal organs.
- It is due to genetic mutations in genes involving the transforming growth factor-β/BMP (bone morphogenic protein) signaling cascade.
- The earliest sign of the disorder is recurrent epistaxis in childhood.
- Characteristic telangiectasias do not appear until early adulthood.
- Telangiectasias are prominent on the tongue, palate, nasal mucosa, palms, soles, and nail beds.
- Most affected people have a normal life span but are at risk for life-threatening hemorrhage.

Hereditary Benign Telangiectasia

- Hereditary benign telangiectasia is an autosomal dominant condition.
- Widespread telangiectasias are found on the skin, but not on the mucosa and internal organs.
- There is no associated bleeding diathesis.

Ataxia Telangiectasia (Louis–Bar Syndrome)

- Ataxia telangiectasia is an autosomal recessive condition with progressive cerebellar ataxia, telangiectasias, and immune dysfunction due to a mutation in the ATM (ataxia telangiectasia mutated) protein.
- The earliest sign—ataxia—is evident when the child begins to walk and usually by the age of 3 years.
- Telangiectasias appear on the conjunctivae, face, neck, and upper trunk by age 5 years.
- Café-au-lait macules, skin ulcerations, poikiloderma, premature gray hair, dry skin, sclerodermatous skin changes, eczema, and hirsutism may also occur.
- People affected by ataxia telangiectasia have defective DNA repair of chromosomal breakages, Kaposi's sarcoma, and an increased sensitivity to ionizing radiation.

Generalized Essential Telangiectasia

- Women are affected more often than men.
- Telangiectasias first appear on the legs and then gradually, progressively, and symmetrically extend to involve the trunk and arms.
- The pathogenesis is unknown.

Unilateral Nevoid Telangiectasia

- There is a unilateral dermatomal distribution of fine telangiectasias.
- The trigeminal and the third and fourth cervical nerves are the most commonly affected dermatomes.
- This condition may be congenital or acquired.
- The congenital form affects males more often, whereas the acquired form is seen more often in females.
- Estrogen may play a role in the acquired form because it can begin during puberty and pregnancy and resolve in adulthood and after delivery.

Secondary Telangiectasias

- Telangiectasias are seen in basal cell carcinoma, rosacea, collagen vascular disorders, corticosteroid atrophy, and chronic graft-versus-host disease.

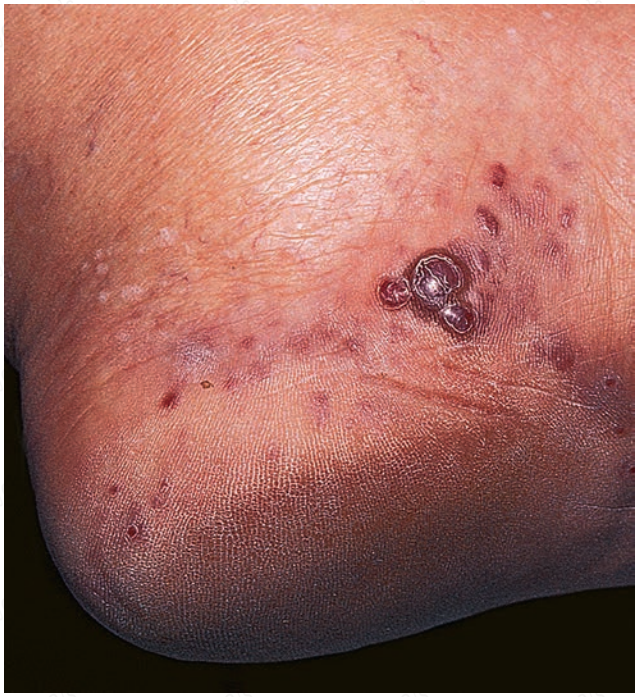

Fig. 19.35 Classic Kaposi's sarcoma typically appears as nodules on the lower legs. These enlarge into dome-shaped tumors.

Fig. 19.36 AIDS-related Kaposi's sarcoma. Flat, deep-purple plaques are the initial presentation. These will become elevated and evolve into nodules.

- Secondary telangiectasias occur in the setting of altered dermal connective tissue as a result of injury or chronic inflammation.
- Damage may be from ultraviolet radiation (actinic damage), ionizing radiation, or treatment with topical or intralesional corticosteroids.
- Telangiectasias occur in scleroderma and the CREST syndrome.

Fig. 19.37 Generalized essential telangiectasia is seen primarily in women. The telangiectasias slowly progress over years and are not accompanied by associated systemic problems.

- Telangiectasias in scleroderma and the CREST syndrome appear as discrete, 5-mm macular clusters—referred to as telangiectatic mats—on the face, lips, neck, upper trunk, and dorsal and palmar aspects of the hands.
- The skin of the fingers feels waxy, and Raynaud's phenomenon, cutaneous calcinosis, and ulceration may be present.

Skin Findings

- The lesion is a dilated dermal vessel with a diameter of 1 mm or less. It is not palpable and is easily blanched with diascopy.
- Lesions may appear as discrete vessels or clustered as telangiectatic mats.
- The distribution of lesions varies according to the underlying condition.

Nonskin Findings

- In hereditary hemorrhagic telangiectasia syndrome, the telangiectasias and arteriovenous fistulas may involve the gastrointestinal tract, liver, brain, and lungs; bleeding from the gastrointestinal tract may present as melena, or more insidiously as anemia.
- Patients with ataxia telangiectasia develop progressive cerebellar ataxia and severe respiratory tract infections, and are at risk for lymphoreticular malignancy.
- Telangiectasias can occur in the setting of occult liver disease.

Fig. 19.38 Hereditary hemorrhagic telangiectasia is an autosomal dominant inherited malformation of blood vessels. Few to numerous lesions occur primarily on the lips, tongue, nasal mucosa, forearms, hands, and fingers and throughout the gastrointestinal tract.

Fig. 19.39 Unilateral nevoid telangiectasia syndrome. Telangiectasias appear in a segmental distribution. The acquired form begins with states of increasing estrogen blood levels: (1) at puberty in females, (2) during pregnancy, or (3) with alcoholic cirrhosis.

Fig. 19.40 The telangiectasias of CREST syndrome and scleroderma occur as flat (macular) 0.5-cm rectangular collections of uniform tiny vessels; these are the so-called telangiectatic mats.

Laboratory and Pathology

- Skin biopsy reveals a thin-walled vessel in close approximation to the overlying epidermis.
- A sparse infiltrate of lymphocytes is often seen surrounding the vessels in hereditary hemorrhagic telangiectasia.
- Depending on the clinical setting and suspicion, diagnosis-specific testing may be indicated.
- Imaging studies of the brain and internal organs should be considered for hereditary hemorrhagic telangiectasia.
- Specific serologic testing is indicated when scleroderma is suspected.

- Autoantibodies directed against centromere proteins are found in a high number of patients with the CREST syndrome; and autoantibodies to DNA topoisomerase type I are found in a high number of patients with diffuse scleroderma.

Differential Diagnosis

- Diagnosis is usually straightforward
- Petechiae may resemble small telangiectasia

Discussion

- Telangiectasias are easily overlooked; lesions occur in a wide range of disorders.
- Distinguishing between primary and secondary disorders narrows the differential diagnosis.

Treatment

- Cosmetically objectionable telangiectasias may be ablated with laser surgery or pinpoint electrocautery.
- Individual lesions may require several treatments.

Pearls

- Careful attention of the distribution, age of onset, and clinical progression of telangiectasias is needed because these may provide useful diagnostic clues to underlying disease.

Spider Angioma (Nevus Araneus)

Description

- Spider angioma is an asymptomatic blanchable pink papule due to a central dilated arteriole and very fine radial branches.

History

- Spider angiomas are found in 10% to 15% of normal adults and children.
- Lesions represent dilations of a previously existing vessel rather than a neoplasm.

Skin Findings

- There is a central, slightly raised, bright-red vascular papule from which fine blood vessels radiate.
- Firm pressure easily blanches the radiating vessels, whereas the central papule is less easily blanched.
- Pulsation of the central papule with this technique confirms the arteriolar nature of the papule.
- Spider angiomas are most commonly found on the face, and also on the neck, upper trunk, and upper arms in adults.
- In children, lesions are also frequently seen on the hands and fingers.

Nonskin Findings

- Spider angiomas occur with increased frequency in pregnancy and in the setting of chronic liver disease.
- It has been suggested that spider angiomas occur in a state of relative estrogen excess.
- Lesions arising during pregnancy tend to resolve after the birth.
- Those found in patients with liver disease are persistent. Other stigmata of chronic liver disease, such as gynecomastia, testicular atrophy, palmar erythema, ascites—and perhaps icterus—may also be present.

Laboratory and Biopsy

- Skin biopsy is rarely indicated but shows a central arteriole ascending into the papillary dermis, giving rise to a subepidermal ampulla.
- Thin-walled arterioles radiate outward into the surrounding papillary dermis and branch into delicate capillaries.
- If chronic liver disease is suggested by clinical examination, laboratory studies to assess hepatic function may be warranted, including viral hepatitis serologies.

Differential Diagnosis

- Small basal cell carcinomas (in adults)
- Telangiectasias (although similar in color and size, they lack the central papule and radiating vessels of spider angiomas)

Course and Prognosis

- Spider angiomas arising during pregnancy and those occurring in children tend to disappear spontaneously over a period of 3 to 4 years.

Treatment

- The patient should be reassured that spider angiomas are common, benign lesions that usually resolve without treatment.
- If the lesion is persistent and cosmetically bothersome, it may be treated with either pulsed dye laser or electrocautery.
- The patient should know that treatment is a cosmetic procedure, there is a slight risk for dyspigmentation and scarring, and lesions may recur.

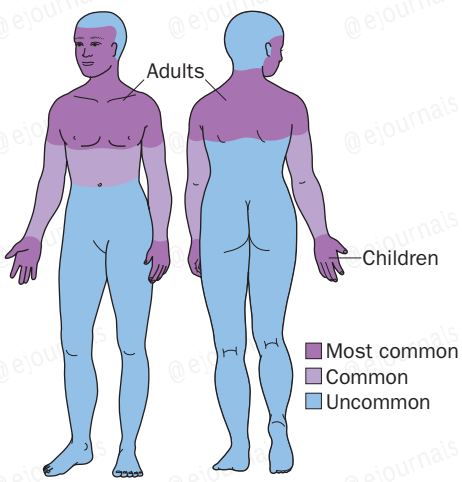

Fig. 19.41 Spider angioma distribution diagram.

- Consultation with a specialist in laser treatment should be considered.

Pearls

- The association between spider angiomas and chronic liver disease is overstated.

Fig. 19.42 Spider angioma. A characteristic central dilated blood vessel with fine radiating blood vessels.

Fig. 19.43 Spider angioma. There is a central vessel with radiating smaller vessels. Firm pressure on the central vessel forces blood out and blanches the lesion.

Fig. 19.44 Spider angiomas form as arterioles (spider bodies) become more prominent near the surface of the skin and radiate capillaries (spider legs). They blanch with firm pressure. They are most common on the exposed surfaces of the face and arms. They increase in number with liver disease and during pregnancy and are probably stimulated by higher than normal concentrations of estrogen.

20 Hair and Nail Diseases

Kathryn A. Zug

Androgenic Alopecia (Male Pattern Baldness)

Description

- Androgenic alopecia is premature loss of hair of the central scalp.

History

- Alopecia is a physiologic reaction induced by androgens in genetically predisposed men.
- The pattern of inheritance is probably polygenic.
- It can begin any time after puberty and usually is fully expressed by the time the patient is in his 40s.

Skin Findings

- Terminal hair follicles are transformed into vellus-like follicles.
- Terminal hair is replaced by fine light vellus hair, which is shorter and has a reduced diameter.
- With time, further atrophy occurs, leaving the scalp shiny and smooth. The follicles disappear.
- It begins with bitemporal thinning that then progresses to an M-shaped recession. Then there is a loss of hair focally in the crown of the scalp, which extends to total hair loss in the central scalp.
- There is increased growth of secondary sexual hair (on the chest, in the axillae, and in pubic and beard areas).

Course and Prognosis

- The progression and various patterns of hair loss have been classified by Hamilton. Triangular frontotemporal recession occurs normally in most young men (type I) and women after puberty. The first signs of balding are increased frontotemporal recession accompanied by midfrontal recession (type II). Hair loss in a round area on the vertex follows, and the density of hair decreases, sometimes rapidly, over the top of the scalp (types III–VII).

Treatment

- Minoxidil (Rogaine) is a topical 2% or 5% (extra strength for men) solution or 5% foam for use in men that is available over the counter.
- It is applied to a dry scalp twice a day. The 5% solution results in greater hair growth.
- Ideal candidates are men younger than 30 years.
- Regrowth takes 8 to 12 months, peaks at 1 year, but can be maintained 5 years later with continued use.
- It may help stop further loss but must be used continually to preserve growth.
- Finasteride (Propecia) at optimal dose of 1 mg/day is an oral prescription medication taken daily. Caution is needed in patients with liver abnormalities.
- The drug works by blocking type II 5α-reductase in hair follicles, lowering serum and scalp levels of dihydrotestostersone, while maintaining testosterone levels.
- Hair growth peaks at 1 to 2 years. Anterior and midscalp and vertex hair loss is improved compared with placebo.
- It must be used daily and chronically to maintain regrowth. One study reported a 21.6% increase in hair weight and a 7.2% increase in hair count from baseline at 192 weeks.
- Decreased libido, ejaculation disorders, orgasm disorders, and erectile dysfunction can continue after discontinuation of the drug, which has a U.S. Food and Drug Administration (FDA) revised label warning.
- Label warnings also include reports of male infertility and of decreased semen quality.

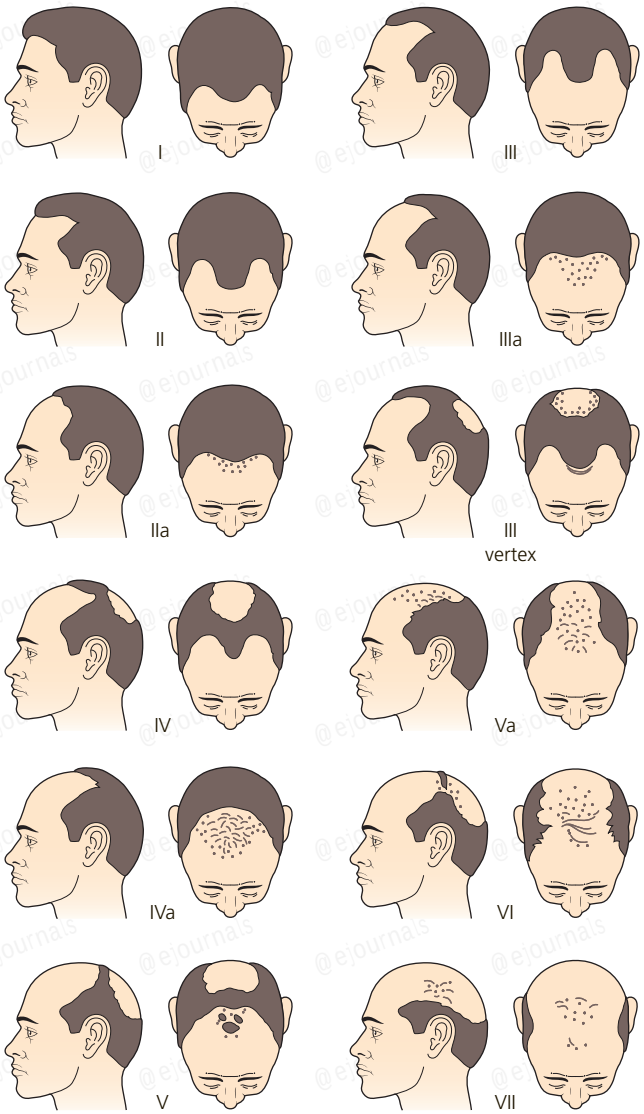

Fig. 20.1 Hamilton classification of male pattern baldness.

- It is Pregnancy Category X and is contraindicated for women of childbearing potential. Feminization of the male fetus is a risk in pregnant patients who take finasteride.
- Dutasteride is another 5α-reductase inhibitor; it is not approved by the FDA for hair loss, and phase III trials for hair loss indication are on hold.
- Hair transplantation has have been used successfully for years to permanently restore hair.
- Hair weaves have been refined in a process whereby strands of human hair are applied to a thin nylon filament anchored to the scalp with the patient's own hair.
- An anteroposterior elliptic excision of bald vertex scalp with primary closure can provide an instant hair effect.

Pearls

- Both finasteride and minoxidil need to be used lifelong for continued efficacy.

- Both finasteride and minoxidil are more likely to be effective if use begins at the earliest onset of hair loss.
- Presently there is limited efficacy of current medical treatments for hair loss. Although the risks of such treatments are minimal, the continued costs and possible sexual dysfunction indicated by expanded FDA labeling may outweigh the benefits.

Fig. 20.2 Thinning of the part-line is seen in androgenetic alopecia in men and in women.

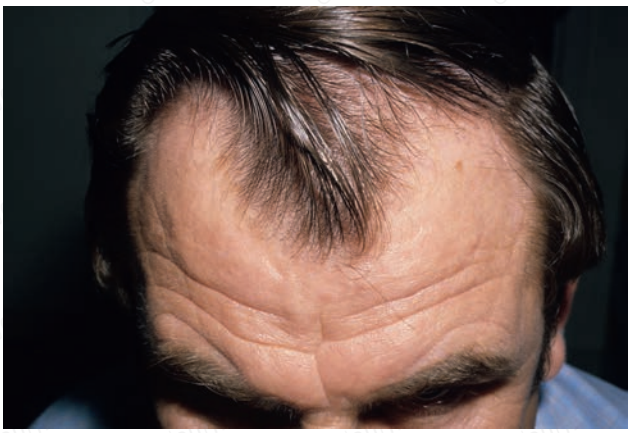

Fig. 20.3 Bitemporal recession is an early sign of androgenetic alopecia.

Androgenetic Alopecia in Women (Female Pattern Hair Loss)

Description

- Androgenetic alopecia in women is a common hereditary, central, diffuse hair thinning that begins at a relatively early age. This is in contrast to postmenopausal hair loss, which begins in women in their 50s, 60s, or 70s. Affected scalp hairs have a shortened anagen cycle and progressive miniaturization of hair follicles.

History

- Inheritance of androgenetic alopecia is poorly understood, although clearly there is genetic predisposition to pattern hair loss. Female pattern hair loss can be early or late onset with or without high androgen levels.
- The true prevalence is unknown, but it may affect 6% to 25% of premenopausal women.
- Women rarely become completely bald like men.
- Hereditary hair thinning begins in the woman's teenage years, 20s, or 30s, and is usually fully expressed by the 40s. There are two peaks of onset: in the 20s and the 40s.
- Hair loss is gradual, not abrupt or massive.
- Menses is normal and regular. Heavy menses causes iron deficiency and increased hair shedding. Pregnancies are normal, and there is no infertility or galactorrhea.
- Certain drugs cause hair thinning. Hair regrows when the drug is stopped.
- Recent discontinuation of an estrogenic oral contraceptive may lead to hair loss.
- Contraceptives containing androgenic progestins (nortestosterone derivatives, e.g., levonorgestrel) may cause or prolong androgenetic alopecia. This is a side effect of levonorgestrel-releasing implants.
- The gonadotropin-releasing hormone antagonists triptorelin and goserelin, the oral esterified estrogen methyltestosterone used for menopause symptoms, and the nonsteroidal aromatase inhibitors letrozole and vorozole used for hormone-sensitive breast cancer may lead to androgenetic alopecia.

Skin Findings

- Most women experience a gradual loss of hair on the central top of the scalp, with retention of the normal hairline without frontotemporal recession, and the scalp becomes more visible.
- Alopecia in frontovertical and temporoparietal supra-auricular areas may occur in some, resulting in a "Christmas tree" form of alopecia anteriorly.
- There is increased spacing between hairs, often pencil eraser–sized areas lacking visible hairs.
- There are a variety of hair diameters in the central scalp. Many of the hairs are miniaturized (thin and short). Hairs along the frontal hairline are normal.
- Hair diameters become thinner over time. This is noticed when the hair is gathered into a ponytail.

Laboratory

- Baseline laboratory tests to rule out medical causes of hair loss include evaluation for thyroid disease, iron deficiency, and connective tissue disease. It is reasonable to check the antinuclear antibody level for connective tissue disease.
- The level of thyroid-stimulating hormone should be determined to rule out a treatable thyroid disease.
- Patients with heavy menses should have the following tests: serum iron determination, total iron-binding capacity, and ferritin level. Replacement of low iron state may be helpful.
- Most patients do not require hormonal evaluation. Most women have no signs of hyperandrogenemia and have normal serum androgen levels; however, 5-alpha DHT, dehydroepiandrosterone sulfate (DHEAS), serum free testosterone, 17-beta-hydroxyprogesterone, delta-4-androstenedione, sex hormone–binding globulin, and cortisol and prolactin levels should be determined if one or more of the following is present: irregular menses, hirsutism, virilization, acne, galactorrhea, or infertility. A subset of women may have polycystic ovarian disease (PCOS) and insulin resistance. A ratio of luteining

hormone to follicle-stimulating hormone (LH:FSH ratio) greater than or equal to 3 is typical of PCOS.
- Scalp biopsy is performed in patients suspected of having a scarring alopecia. Biopsy is sometimes performed to rule out the diffuse form of alopecia areata or telogen effluvium.

Treatment

- The term "female pattern baldness" should be avoided. Instead, the term "female pattern hair loss" should be used when talking to patients.
- Topical minoxidil 2% solution (Rogaine) is the standard treatment and may be effective in some women. It is applied twice a day for a trial of 6 months. If effective, it must be continued for persistent effect. If there is no response, the 5% solution may be tried twice daily. The 5% solution is approved for use in men. It may result in unwanted facial hair.
- Patients with abnormal laboratory studies can be referred to an endocrinologist or a gynecologist.
- There are no restrictions on frequency of washing, combing, hair coloring, or permanents.
- Estrogen is not prescribed to treat women for androgenetic alopecia.
- Spironolactone is sometimes used in divided doses of 50 to 200 mg/day; it is Pregnancy Category D and may elevate serum potassium.
- Although finasteride is helpful in men, in women a dose of 1 mg daily was not beneficial in a 1-year study of 137 postmenopausal women. It may be more helpful in women with hyperandrogenism.
- Women with androgenetic alopecia who desire an oral contraceptive should use a progestin with little androgenic activity—such as norgestimate or desogestrel. One study reports an increased hair growth in postmenopausal women taking finasteride 2.5 mg/day in combination with an oral contraceptive pill containing drospirenone and ethinyl estradiol.

Pearls

- Hair loss is a common complaint in women and can be emotionally devastating.
- Widening of the "Christmas tree" pattern of loss is evident with hair loss of the frontal scalp exceeding loss of the occiput. This part is often the earliest visible change. Diffuse thinning and hair shedding occur, most commonly after menopause.

Fig. 20.4 Female pattern hair loss. Ludwig pattern showing evolution of the female type of androgenetic alopecia.

Fig. 20.5 Female pattern hair loss. Widening of the part on top is notable initial change; compare this with the patient's temporal scalp, where hair density is greater.

Fig. 20.6 Female pattern hair loss. Female patients with this pattern of hair loss note it readily because hair density is less and the scalp is more readily seen. The change is typically gradual over years.

Telogen Effluvium

Description

- Telogen effluvium is a nonscarring, noninflammatory, diffuse hair loss (alopecia) that is typically sudden in onset and occurs 3 to 5 months after a systemic stress, such as childbirth, a severe medical illness, crash dieting, severe stressors, surgery, and high fever and occasionally in response to medication.

History

- Telogen effluvium may be acute or chronic. The acute form occurs abruptly after a specific trigger and is of less than 12 months' duration.
- Chronic telogen effluvium may or may not have an identifiable inciting stressor; it may be acute or slow in onset and greater than 12 months' duration.
- The hair loss is often most noted by the patient as clumps of hair coming out in the shower or in the hairbrush.
- The quantity of hair lost each day is often dramatic, very noticeable, and distressing to the patient; however, such loss may not be easily detected on direct inspection by others.
- The hair loss typically occurs 3 months after the inciting stressor because the loss is a result of anagen (growing-phase) hairs shifting abruptly into catagen (the apoptotic stage), and then into telogen (resting-phase) when the hair is lost.
- Not all anagen hairs undergo this stage shift; the quantity of hairs shifting stage determines the amount of loss.
- The most common form of telogen effluvium results from early conversion of hairs to telogen phase, as noted associated with systemic stress, such as surgery, major illness, and crash dieting. The hair loss occurs 3 to 5 months after the major stress.
- Telogen effluvium can also be caused by a delayed anagen release, whereby affected hairs are delayed in their conversion to telogen hairs; this type of telogen effluvium occurs after childbirth. When delayed anagen release occurs, hairs cycle into telogen and are shed 3 to 5 months later.
- Drug-induced telogen effluvium is the most common drug-induced hair loss. Most drugs do this by causing the follicle to prematurely arrest and cease growth. There are many drugs associated with hair loss. Severe hair shedding (>200–300 hairs a day) is uncommon but can be seen in patients taking interferons, heparin, and antineoplastic agents. Onset is typically within days to weeks of new medication introduction or dosage increase.
- Chronic telogen effluvium is believed to be caused by a short anagen cycle. Affected patients are typically middle-aged women with thick hair before onset of shedding.
- Hair loss in infants occurs between birth and 4 months; regrowth is typical by 6 months.

Skin Findings

- The scalp hairs are primarily affected; the density of hairs is variably reduced. Early on, the reduction in hair density may be undetectable by the clinician.
- The hair density as manifest by the part width is similar at the occiput and at the crown.
- Pull test is positive: gentle pulling of hair clumps in multiple regions of the scalp will yield more than two or three telogen (club) hairs per pull.
- Bitemporal thinning may be observed.

Nonskin Findings

- The fingernails may show horizontal ridges (Beau's lines) that indicate a similar growth arrest occurring several months previously.

Laboratory

- Hair pluck is an uncomfortable test in which at least 10 hairs are plucked from the scalp. Examination of the hair bulbs using light microscopy will yield an increased telogen-to-anagen ratio above the normal ratio of 1 : 10. This test is rarely required for diagnosis and is uncomfortable for the patient.
- Biopsy is not typically indicated if the clinical findings and history are supportive. Biopsy shows an increased number of telogen and catagen follicles, but no

inflammation or miniaturization of hair follicles. A 4-mm punch biopsy for horizontal sectioning should show between 25 and 50 hairs; more than 12% to 15% of the hairs would be in telogen.
- Consider the ratio of iron to total iron-binding capacity. Ferritin may be low in patients with anemia, vegetarians, or those with a history of heavy menstrual cycles.
- Anorexia, crash dieting, or dramatic weight loss may manifest as low ferritin, albumin, and total protein.
- Thyroid function tests are indicated if symptoms or signs of thyroid disease are present.

Course and Prognosis

- This form of hair loss does not affect all hairs; thus, the loss of hairs is never total.
- Regrowth of hairs occurs in 95% by 12 months; there is no scarring or permanent loss.
- Sometimes regrowth occurs during a time when the affected patient is also experiencing hair loss due to miniaturization of hairs as occurs in androgenetic alopecia; in this case, regrowth of hair may not appear as complete.
- The course of chronic telogen effluvium is unpredictable. It is often waxing and waning and may last several months to several years.

Differential Diagnosis

- Androgenetic alopecia
- Diffuse form of alopecia areata (biopsy may be necessary)
- Loose anagen hair syndrome (the pull test should yield some anagen hairs)

Treatment

- Spontaneous regrowth is the rule.
- No treatment is likely to shorten the course or hasten regrowth.
- If medications are responsible, they should be discontinued if possible. The list of medications is long and includes anticoagulants, beta-blockers and angiotensin-converting enzyme inhibitors, hormones, anticonvulsants, lithium, and others.
- The most important aspect of treatment is an emotionally supportive relationship during the evaluation, diagnosis, and follow-up.
- Education of the patient regarding hair cycle dynamics, the short arrest in growth due to a specific stressor, and the likelihood of regrowth are helpful and reassuring details to discuss.
- Minoxidil 5% solution applied twice daily may be helpful for chronic telogen effluvium.

Pearls

- Understanding the hair cycle is important for understanding the dynamics of telogen effluvium. Hair loss is emotionally traumatizing; support and reassure the patient that this form of hair loss has an excellent prognosis for complete regrowth.
- Weekly hair collection may also be very reassuring by demonstrating that the hair loss is diminishing with time.
- Ask the patient to collect all hairs lost in the shower, on the pillow, and on the hair brush once weekly in the morning. The hairs are put in a labeled plastic bag, and the quantity is compared over time.
- Medications associated with telogen effluvium include amphetamines, captopril, anticoagulants, antiretroviral drugs (indinavir), fluoxetine, dopaminergic therapy for Parkinson's disease, cimetidine, enalapril, etretinate, lithium, metoprolol, and propranolol. Oral contraceptive therapy discontinuation may provoke telogen effluvium.

Hair Facts and Hair Cycle Dynamics

- Human hair growth is dynamic; the growth of hairs on the scalp is mosaic (hairs are cycling through anagen, catagen, and telogen phases; the growth cycle phase of individual hairs is variable).
- Anagen phase is the growing phase. Approximately 85% to 90% of all hairs are in anagen, and it lasts roughly 3 years.
- Catagen phase is the transitional, apoptotic phase. Roughly 3% to 5% of hairs are in catagen. It lasts roughly 1 to 2 weeks.

- Telogen phase is the resting phase, in which 5% to 10% of hairs are in telogen. The duration is roughly 3 months.
- The normal number of scalp hairs is 100,000.
- The average number of hairs shed per day is 100 to 150.
- The normal anagen-to-telogen ratio in a "hair pluck" is 9:1.

Scalp Biopsy Mechanics

- Scalp biopsy specimen for alopecia should be taken near the edge of the affected region. A punch biopsy should be taken on an angle parallel to hair growth. One punch biopsy can be submitted whole for standard transverse sectioning. A second punch biopsy, using a 4-, 5-, or 6-mm punch, can be bisected horizontally about 1 mm above the dermal–subcutaneous junction. Each piece is then embedded cut-side down by the pathologist. Serial horizontal sections can then be performed and are best read by a pathologist who is experienced in reading horizontal scalp biopsies.

Alopecia Areata

Description

- Alopecia areata is a nonscarring hair loss, typically of rapid onset in a sharply defined, usually round or oval area.
- The loss may be diffuse, patchy, or band-like at the margins of the scalp.
- It is likely to be due to an immunologic phenomenon; T lymphocytes appear to play an important pathogenic role.
- The triggering cause is unknown. Genetic susceptibility plays a role. Hair follicle danger signals attract specific T cells to the hair follicles, resulting in immunologic damage.
- Hair loss can be emotionally devastating, and low self-esteem, anxiety, and depression are common consequences that should be carefully addressed early and throughout the course.

History

- Alopecia areata is most common in children and young adults.
- There is a sudden occurrence of one or several areas of hair loss of 1 to 4 cm.
- The eyelashes and beard may be involved, and—rarely—other parts of the body.
- Total hair loss of the scalp (alopecia totalis) is seen most frequently in young people; it may be accompanied by cycles of growth and loss.
- Total hair loss of the body (alopecia universalis) is rare.
- Stress is frequently cited as the cause, but there is little evidence that it plays a role.
- Regrowth begins in 1 to 3 months and may be followed by loss in other areas.
- The prognosis for total permanent regrowth in cases with limited involvement is good, but it is poorer for patients with more involvement.
- Alopecia areata has been reported to develop during tumor necrosis factor-alpha inhibitor therapy (etanercept, infliximab, adalimumab).

Skin Findings

- A wide spectrum of involvement is seen. The most common pattern is patchy. Other patterns include the ophiasis pattern (a band-like loss at the scalp margins) and the ophiasis inversus pattern (spares the periphery of the scalp while involving the crown).
- The diffuse pattern is the least common, in which there is decreased hair density throughout the scalp.
- The skin is typically very smooth, or may have short stubs of hair.
- The hair shaft is poorly formed and breaks on reaching the surface. Tapered hairs resembling exclamation points may be best seen at the margin of an area of loss.
- New hair is usually the same color and texture, but may be fine and white.

Nonskin Findings

- Structural and functional abnormalities of the thyroid may occur.
- Diffuse fine nail pitting occurs in up to 30% of cases.

Laboratory

- Biopsy of affected scalp may be performed if the clinical presentation is not typical. Biopsy findings include peribulbar lymphocytes, miniaturized follicles, a telogen-to-vellus hair ratio of 1.5:1, and increased telogen and catagen follicles. The presence of eosinophils in a biopsy is a helpful diagnostic sign in cases that are difficult to diagnose.

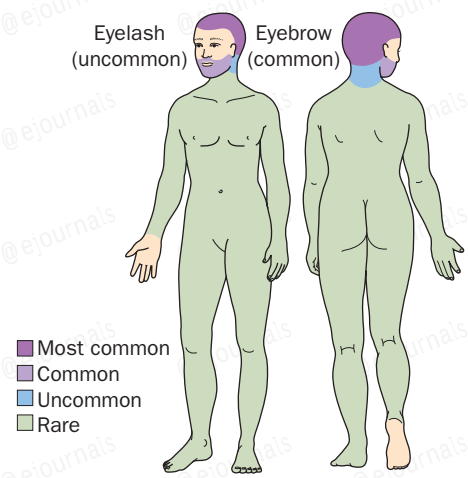

Fig. 20.7 Alopecia areata distribution diagram.

- Alopecia areata may be associated with thyroid disease, pernicious anemia, Addison's disease, vitiligo, lupus erythematosus, ulcerative colitis, diabetes mellitus, and Down syndrome.
- Tri-iodothyronine, thyroxine, thyroid-stimulating hormone, antithyroglobulin, and antimicrosomal antibody testing should be considered, especially for children.

Differential Diagnosis

- Trichotillomania
- Tinea capitus
- Syphilis
- Telogen effluvium
- Androgenic alopecia

Treatment

- In most areas, hair regrows, and no treatment is needed.
- Group I topical steroids applied twice a day are minimally effective. They should be used in cycles, such as 2 weeks of treatment and 1 week of no treatment.
- Intradermal injection of triamcinolone acetonide (Kenalog) 2.5 to 10 mg/mL is effective.
- Injections may be repeated at 4-week intervals.
- Atrophy is the major side effect.
- This treatment should be reserved for patients with a few small areas of hair loss.
- Anthralin (Drithocreme 1%, 0.5%, 0.25%, or 0.1%), applied once a day in concentrations high enough to induce a visible dermatitis, is occasionally effective.
- Squaric acid dibutyl ester is used by some specialists; sensitization is generally with a 2% concentration to an area of 4 cm, waiting 2 weeks for sensitization, followed by application of 0.001% in children and 0.01% in adults applied to affected areas, three or four times a week. Such contact allergy can be severe, however.
- An intravenous pulse of methylprednisolone may be effective in patients with rapidly progressing extensive multifocal alopecia areata.
- Oral corticosteroid therapy does not prevent the spread or relapse of severe alopecia areata, and when regrowth is obtained, it is rarely maintained off-therapy.
- Promising research is underway on use of Janus kinase (JAK) inhibitors (ruxolitinib and tofacitinib), which block important immune pathways as a potential treatment for moderate to severe alopecia areata. Side effects, costs may limit use. Topical versions are also being investigated.
- A hair prosthesis should be considered and encouraged for patients with diffuse loss when emotional distress is high.
- A network of support groups across the country is available to help patients cope, e.g., the Alopecia Areata Foundation (http://www.naaf.org).

Pearls

- Patients with a diffuse pattern of alopecia areata are panicked by the marked diffuse hair shedding, which is rapid and progressive. Gentle hair pull in these patients reveals more than 10 hairs per pull, consisting of dystrophic anagen hairs or telogen hairs.
- The National Alopecia Areata Foundation (http://www.naaf.org) is a vital resource for patients and physicians for support, information, and research.

Pediatric Considerations

- Hair loss at any age is emotionally distressing but is particularly challenging and upsetting for children. Emotional support and encouragement are essential. Counseling may be indicated.
- Most children with localized alopecia areata will regrow hair in the affected regions within 1 year.
- If intralesional injections are used in children, they should be for limited areas of loss only and of low strength (2.5–5 mg/mL Kenalog intralesionally). EMLA topical anesthetic can be applied 2 hours before injection of the affected area to diminish the pain of injection.

Fig. 20.8 A, Classic appearance of alopecia areata with sharply demarcated, round, hairless patches without inflammation and without scarring. **B,** "Exclamation point" hairs seen under magnification. Note the tapered appearance—fat distally and thin, narrowed base of hairs.

Fig. 20.9 Alopecia areata is characterized by the rapid onset of total hair loss in a sharply defined, usually round area. The duration and extent of loss varies greatly. Most cases are asymptomatic, but a few patients complain of burning. The skin feels smooth.

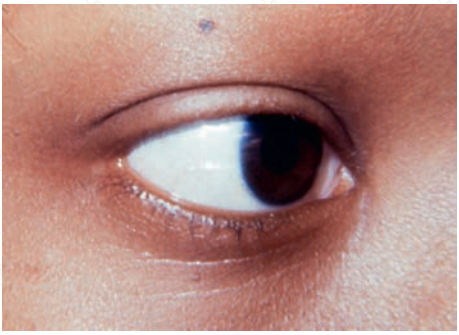

Fig. 20.10 Loss of eyebrows and eyelashes may be partial or complete in alopecia areata. Unlike the scalp where a hair prosthesis can be easily worn, this area is more difficult for patients to emulate a natural appearance.

Fig. 20.11 Alopecia areata. A wide spectrum of involvement is seen. Most patients report the sudden occurrence of one or several 1- to 4-cm areas of hair loss on the scalp.

Fig. 20.12 Alopecia totalis. All or near total loss of hair occurs in about 5% of all alopecia areata cases. Loss is sudden.

Trichotillomania

Description

- Trichotillomania is the recurrent pulling of one's hair, which results in significant hair loss. The urge to pull hair is overwhelming; after hair pulling, anxiety is relieved temporarily.
- It may involve many hours each day of pulling the hair—or thinking about pulling it.
- Often the "puller" does not admit to this habit.

History

- Trichotillomania is a habit tic most commonly found in young children.
- It is also seen in adolescents and adults.
- The female-to-male ratio is 2.5:1.
- Hair is twisted around the finger, pulled, and rubbed until it is extracted or broken.
- Favorite sites are the easily reached areas—the frontoparietal scalp, eyebrows, and eyelashes.
- It first manifests during inactive periods, perhaps while watching television, or before falling asleep.
- Parents seldom notice the behavior.
- It is often associated with underlying anxiety, depression, and low self-esteem.
- It can be a chronic problem, and it often resolves spontaneously.

Skin Findings

- There is a patch of hair loss with an irregular, angulated border.
- The hair density is greatly reduced; the involved area is not completely bald and smooth like in alopecia areas.
- Short, broken hairs of varying lengths are randomly distributed in the involved site.

Laboratory

- Potassium hydroxide test rules out noninflammatory tinea capitis.
- Plucked hair shows no telogen hair roots (100% in the active growing anagen phase).
- Gentle hair traction produces no more hair loss.
- Skin biopsy reveals a marked increase in catagen hairs.

Differential Diagnosis

- Alopecia areata
- Tinea capitis
- Syphilis

Treatment

- Treatment is often delayed, or not sought, because of embarrassment.
- Response is best to combination therapy including psychopharmacology, psychotherapy, and behavior modification (e.g., habit substitution), rather than psychotherapy alone.
- The child's attention should be diverted when hair is being pulled.
- The parents and physician should be accepting and supportive rather than judgmental and punitive.

Fig. 20.13 Trichotillomania. The favorite site is the easily reached frontoparietal region of the scalp, but any scalp area, or the eyebrows and eyelashes, may be attacked.

- Extensive involvement or persistence requires psychiatric evaluation. Psychotherapy can be helpful.
- Trichotillomania shares features with obsessive–compulsive disorder, including response to medication.
- Clomipramine (Anafranil), fluoxetine (Prozac), and pimozide (Orap) can be effective; however, not all patients respond fully to psychopharmacology alone.

Pearls

- The favorite site is the easily reached frontoparietal region of the scalp, but any scalp area or the eyebrows and eyelashes may be attacked.
- The affected area has an irregular, angulated border, and the density of hair is greatly reduced, but the site is never bald as in alopecia areata.
- Multiple visits to providers and specialists seeking a diagnostic answer are typical for this condition; a biopsy can be helpful and supportive of this diagnosis.

Pediatric Considerations

- This condition is most commonly seen in children. A careful social history seeking sources of distress or emotional difficulties is advised.
- Discussion with an understanding physician or parent is most helpful for the affected child. Referral for psychiatric evaluation and consideration for behavioral and pharmacologic therapy may be delicate but is highly recommended.

Fig. 20.14 Several short broken hairs of varying lengths are randomly distributed in the involved site. Hair that grows beyond 0.5 to 1 cm can be grasped by small fingers and extracted.

Fig. 20.15 Large, rounded area of hair loss, but with obvious central regrowth. The differential diagnosis is alopecia areata. The patient should be asked about manipulation of the hair. No hairs are released with gentle hair pull. In a hair pluck, trichotillomania shows no telogen hair roots; anagen hairs make up nearly 100%.

Nail Diseases

Anatomy

- The nail plate is hard, translucent, dead keratin.
- The nail fold includes the skin surrounding the lateral and proximal aspects of the nail plate. The proximal nail fold overlies the matrix. Its keratin layer extends onto the proximal nail plate to form the cuticle.
- The matrix synthesizes 90% of the nail plate. The lunula (white half-moon), which is visible through the nail plate, is the distal aspect of the nail matrix.
- The nail bed extends from the distal nail matrix to the hyponychium. The nail bed consists of parallel longitudinal ridges with small blood vessels at their base. Bleeding induced by trauma or vessel disease occurs in the depths of these grooves, producing the splinter hemorrhage pattern.
- The hyponychium is a short segment of skin lacking nail cover; it begins at the distal nail bed and terminates at the distal groove.

Growth Rates

- Fingernails grow at a rate of 0.5 to 1.29 mm per week. It takes approximately 5.5 months for a fingernail to grow from the matrix to the free edge.
- Toenails take 12 to 18 months to be replaced.
- A reduction in the rate of matrix-cell division occurs during systemic diseases, such as scarlet fever, causing thinning of the nail plate (Beau's lines).
- Nail growth rate decreases with age and poor circulation.

Nail Biopsy

- Nail biopsies are usually performed by specialists.
- Nail biopsies are used to diagnosis tumors, inflammatory disease, and infections.
- The ideal ungual biopsy is performed after avulsion of the plate. This allows clear visualization of the matrix and bed.
- A punch or excisional biopsy technique is chosen, which provides a sufficient amount of tissue and produces a minimal amount of scarring.

Ridging and Beading

- Longitudinal ridging is a common aging change that is occasionally seen in young people.
- Beading occurs at all ages but is more common in elderly people. The beads cover part or most of the plate surface and are arranged longitudinally.
- Patients may sand or buff the nail to smooth the surface. Elon nail conditioner (http://www.ilovemynails.com) prevents dryness and cracking.

Fig. 20.16 Nail diseases. Ridging and beading are an aging change. Both beads and ridges appear in this nail.

Fig. 20.17 Age-related longitudinal ridges and beads.

Onycholysis

- Onycholysis is the separation of the nail from the nail bed. It is more common in women with long nails. Vigorous cleaning under the nail accelerates the process.
- Separation begins at the distal end and slowly progresses proximally.
- The nonadherent portion of the nail is white, yellow, or green-tinged.
- Causes include psoriasis, trauma to long nails, *Candida* or *Pseudomonas* species infections, internal drugs (tetracyclines, fluoroquinolones), contact with chemicals, maceration from prolonged immersion in water, and allergic contact dermatitis (e.g., to nail hardener or adhesives).
- Screen patients with unexplained onycholysis for hyperthyroidism, asymptomatic thyroid disease, and iron deficiency.
- Treat by cutting the separated portion of the nail. This promotes dryness and discourages infection. Do not soak the fingertip.
- Avoid exposure to contact irritants.
- Yeast grows in the space between the nail and nail bed. Use liquid topical agents (e.g., fungoid tincture that contains miconazole). Consider oral fluconazole for resistant cases. A short course of fluconazole (e.g., 150 mg every day for 5–7 days) may have to be repeated as the nail grows out.

Fig. 20.18 Onycholysis occurring in a woman with long nails. The separated nails appear yellow or white. Patients think they have a fungal nail infection.

Fig. 20.20 Onycholysis has several causes, including nail trauma, repeated wet work, vigorous repeated manicuring, acrylate (false nail) allergy, and psoriasis. This patient has onycholysis from psoriasis.

Fig. 20.19 Onycholysis is separation of the nail plate from the nail bed. It is common in women with long nails. Low-grade repeated pressure on the distal plate lifts the nail.

Fig. 20.21 Central horizontal stacked depressions in the nail plate occur because of repeat trauma to the proximal nail fold. This is most often seen on the thumb and is a result a repeated flicking, fidgeting, or picking at the skin of the proximal nail fold.

Habit-Tic Deformity

- Biting or picking a section of the proximal nail fold of the thumb with the index fingernail is a common habit. Other nails can be affected.
- Linear bands of horizontal grooves extend up the nail surface. Nail rippling from chronic eczema of the proximal nail fold causes a similar appearance.
- Patients who can stop this habit will eventually regrow normal nails.

Psoriasis

- The incidence of nail involvement in psoriasis varies from 10% to 50%.
- Nail involvement may be the only sign of psoriasis, but it usually occurs simultaneously with skin disease. One or several nails may be involved.
- Pain may restrict activities.
- Pitting is the most common finding. There may be a few or many pits, and they are haphazardly distributed on the surface.
- Onycholysis is separation of the nail from the nail bed. Separation begins at the distal groove or under the nail plate and may involve several nails. The separated nail appears yellow and is often misinterpreted as a fungal infection.
- Subungual scaly debris may accumulate under the distal nail plate. The yellow-white debris elevates the distal nail. This also is commonly mistaken for nail fungus infection.
- Surface distortion of the nail plate occurs when psoriasis affects the nail matrix.
- Oil spot lesions are yellow-brown spots seen through the nail surface. Psoriasis of the nail bed causes serum and scaling debris to accumulate under the nail plate.
- Treatment of skin disease with systemic agents such as cyclosporine, methotrexate, or acitretin will improve the nails.
- Many topical agents (calcipotriol, tazarotene, and anthralin) have been tried, but results are discouraging. Intralesional injections at monthly intervals into the matrix and lateral nail folds are effective but painful. Triamcinolone acetonide (Kenalog) 2.5–5 mg/mL is delivered with a 30-gauge needle. The procedure is painful, and most patients do not continue.

Fig. 20.22 Pitting is the most characteristic sign of psoriasis of the nail plate. Look at all of the other nails for other signs of psoriasis. Patients with nail psoriasis may have no skin disease.

Fig. 20.23 Psoriasis (oil spot lesion). Psoriasis of the nail bed under the nail plate causes serum to accumulate. This brown stain can be seen through the nail plate and resembles an oil spot.

Fig. 20.24 Matrix involvement leads to a completely dystrophic nail in psoriasis. Nail psoriasis is difficult to treat with topical therapy.

Fig. 20.25 Multiple nails show onycholysis. Activity of psoriasis in the nails and the skin do not reliably correlate.

Acute Paronychia

- Bacterial infection of the proximal and lateral nail fold causes the rapid onset of pain and swelling.
- Trauma and manipulation are the cause, or it may occur spontaneously.
- Pus accumulates behind the cuticle or deeper in the lateral nail folds.
- Pus is drained by inserting the pointed end of a comedone extractor or similar instrument between the nail fold and the nail plate. Pain is abruptly relieved.
- Deeper infections may require incision to drain the abscess.
- Small confined abscesses may respond to just drainage. Larger abscesses with surrounding erythema are treated with antistaphylococcal antibiotics.

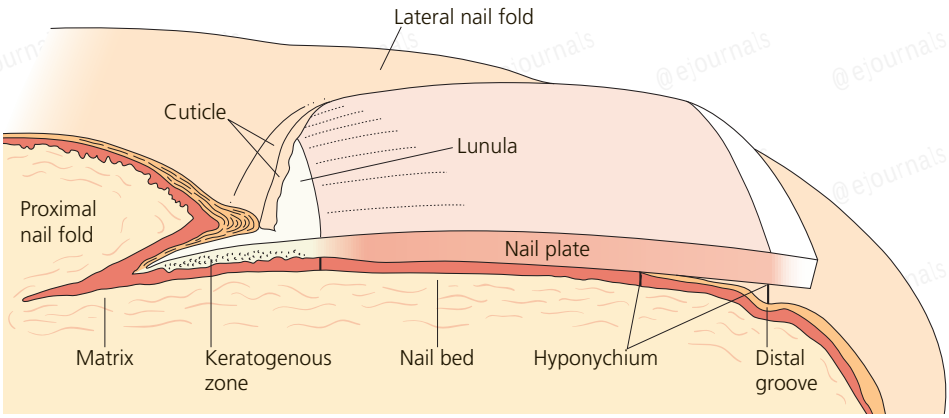

Fig. 20.26 Edema, pus of the nail fold, and surrounding erythema characterize an acute paronychia.

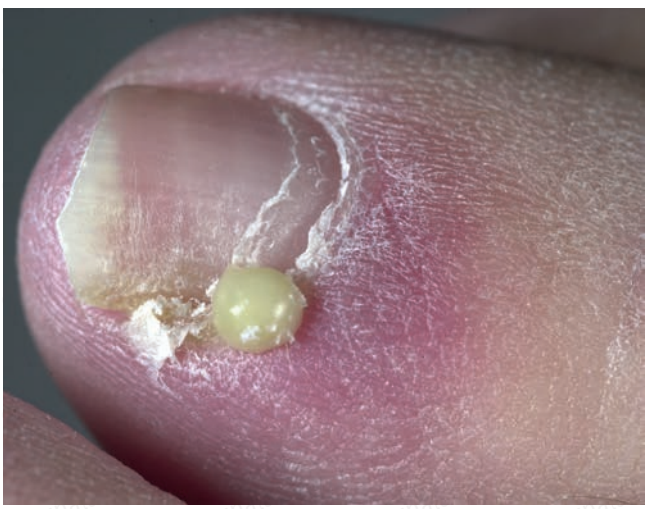

Fig. 20.27 Pain resolves immediately as the pressure is released when pus is evacuated. The cause of acute paronychia is most commonly *Staphylococcus aureus*.

Chronic Paronychia

- Contact irritant exposure is the major cause. Bakers, dishwashers, surgeons, and dentists are at risk. Constant wet work exposure is a risk factor.
- Many or all fingers are involved. There is tenderness, erythema, and mild swelling about the proximal and lateral nail folds.
- The cuticle disappears, leaving the space between the proximal nail fold and the nail plate exposed to infection. Manipulation of the cuticle accelerates the process.
- Both bacteria and yeast grow in the warm moist space under the proximal nail fold. A small quantity of pus can be expressed from under the proximal nail fold.
- Chronic inflammation causes the nail plate to be distorted, but it remains uninfected.
- Psoriasis may have an identical appearance.
- Goals of treatment are to avoid irritation, suppress inflammation, and treat any infection.
- Vinyl gloves, and wearing a cotton glove underneath, afford protection (http://www.allerderm.com).
- Fungoid tincture (miconazole) is applied twice daily to the proximal nail fold and allowed to flow into the space created by the absent cuticle. The cuticle may never reform in patients with long-standing inflammation.
- Fluconazole 150 to 300 mg every week for 4 to 6 weeks may control resistant cases. It is best to limit antifungal use and focus on avoidance of irritants and control of inflammation with topical anti-inflammatory treatment. Short courses of fluconazole may have to be repeated as the infection recurs.

Fig. 20.28 Ragged cuticles and inflammation of the proximal nail folds leads to ridging of the nail plates, typical of chronic paronychia.

Fig. 20.29 Chronic paronychia. The proximal nail fold is erythematous and swollen, and the cuticle is absent. Nail growth is dystrophic because of the chronic inflammation.

Pseudomonas Species Infection

- Separation of the nail plate (onycholysis) exposes a damp, macerated space between the nail plate and the nail bed.
- *Pseudomonas* species thrive in this warm, moist space and stains the undersurface of the nail plate a green-black color. There is little discomfort or inflammation as occurs with subungual hematoma. This is commonly termed "green nail syndrome" or chloronychia.
- Clippings and debris from the nail can be sent for culture.
- Apply a few drops of a bleach mixture (one part chlorine bleach to four parts water) under the nail three times a day. Vinegar (acetic acid) may also be used. Other topical therapy options include gentamicin drops or topical silver sulfadiazine. Delivery to affected area is difficult with topicals. Oral treatment with ciprofloxacin 250 to 500 mg twice daily for 2 weeks will usually cure the infection.
- Cut unattached nail to eliminate the damp space under the nail.

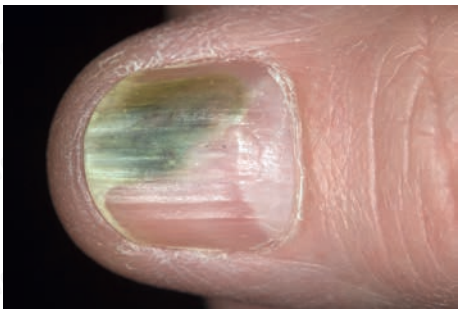

Fig. 29.30 Green discoloration under the nail plate occurs with *Pseudomonas* species infection.

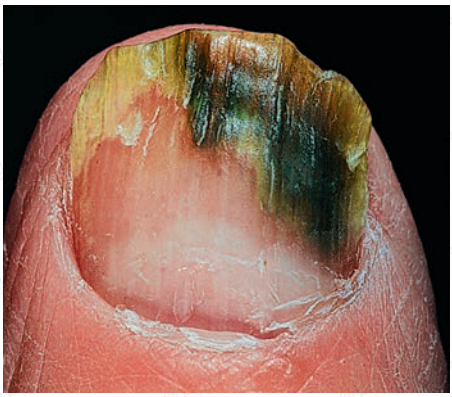

Fig. 20.31 Chronic *Pseudomonas* species infection under the nail plate has caused deep-green pigmentation of the full thickness of the nail plate.

Hangnail

- Triangular strips of skin may separate from the lateral nail folds, particularly during the winter months.
- Attempts at removal may cause pain and extension of the tear into the dermis.
- Separated skin should be cut before extension occurs. Constant lubrication of the fingertips with thick skin creams (e.g., Aquaphor ointment) and avoidance of repeated hand immersion in water is beneficial.

Ingrown Toenail

- Ingrown nails are caused by lateral pressure of poorly fitting shoes, by improper or excessive trimming of the lateral nail plate, or by trauma.
- They occur most often on the large toe. The first signs are pain and swelling.
- The nail pierces the lateral nail fold and enters the dermis, where it acts as a foreign body.
- The area of penetration becomes purulent and edematous as granulation tissue grows alongside the penetrating nail.
- Treatment involves removing the penetrated nail with scissors and curetting the granulation tissue. Small areas of granulation tissue can simply be treated with silver nitrate sticks.
- Cellulitis may occur and need treatment with oral antibiotics.
- Cool wet dressings suppress inflammation and treat swelling.
- Podiatrists treat chronic recurrent ingrown nails by destroying the lateral nail matrix with phenol.

Fig. 20.32 Ingrown nail. The nail plate has penetrated the lateral nail fold. Erythema and swelling occurred. Granulation tissue has appeared at the distal lateral fold.

Subungual Hematoma

- Trauma to the nail plate may cause immediate bleeding and pain.
- Bleeding may cause separation and more pain.
- Puncture the nail surface with a red-hot paperclip tip or 2-mm punch biopsy tool to drain the blood.
- Trauma to the proximal nail fold causes hemorrhage that may not be apparent for days.
- This may mimic melanoma; diagnostic caution is needed. Biopsy if not clear.

Fig. 20.33 Subungual hematoma. Accumulation of blood occurs under the nail plate following trauma. Trauma occurred weeks ago in this patient. The blood has lysed, but the staining will persist until the nail grows out.

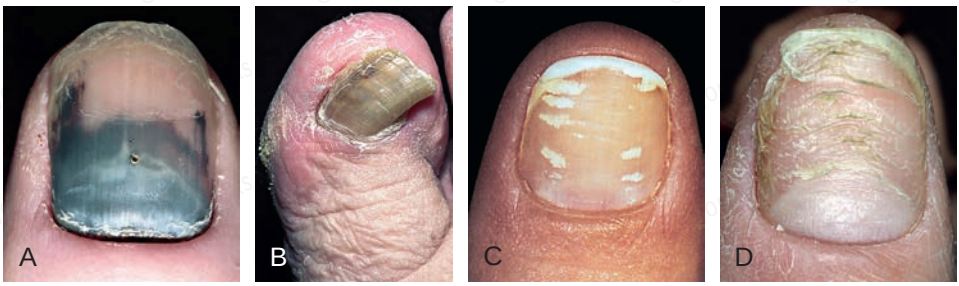

Fig. 20.34 **A,** Patients often do not remember the trauma that produces a sublingual hematoma. If the blood collection is enough, it will result in nail shedding. **B,** Dystrophic distorted nail that has KOH positive subungual debris. **C,** Linear white surface macules can be scraped to look for superficial fungal infection. These white macules may be due to repeated trauma. **D,** This nail shows multiple linear horizontal depressions. Repeated eczematous dermatitis flares of the proximal nail fold area accounts for these changes.

Nail Hypertrophy

- Gross thickening of the nail plate may occur with tight-fitting shoes or other forms of chronic trauma. Pressure on the nail from shoes causes pain with every step.
- Thick nails are often misdiagnosed as a fungal infection.
- The nail plate may be reduced with sandpaper or a file, or the nail can be removed and the nail matrix permanently destroyed with phenol so that the nail will not regrow.

Fig. 20.35 Care must be taken in the evaluation of suspected sublingual hematomas because melanoma can have a similar appearance.

White Spots or Bands

- White spots in the nail plate are common and probably are a result of repeated low-grade trauma.
- The spots or bands eventually grow out and disappear.
- Patients often misinterpret this finding as a fungal infection.

Fig. 20.36 White bands are a common finding and are probably caused by low-grade trauma to the proximal nail fold.

Fig. 20.37 Distal nail splitting is analogous to dry skin. The distal plate separates into layers and peels away. Wetting the hand repeatedly exacerbates the problem.

Fig. 20.38 High fever, systemic illness, and chemotherapy are among the causes of a transient arrest in nail growth. The result is Beau's lines—horizontal nail dents across all nails. This line moves out distally with nail growth.

Distal Plate Splitting (Onychoschizia)

- Brittle nails and splitting are found in 20% of adults and are more common in women.
- Frequent wet work is a common cause.
- The splitting into layers or peeling of the distal nail plate resembles the scaling of dry skin.
- Nails—like the skin—dry in the winter. Repeated water immersion encourages the process. Vinyl gloves protect during wet work.
- Rehydrate the nail by soaking in water. Then apply a thick lubricant such as Aquaphor ointment or Elon nail conditioner (http://www.ilovemynails.com). These are found in some pharmacies.

Beau's Lines

- Beau's lines are transverse depressions or ridges of all of the nails that appear at the base of the lunula weeks after a stressful event has temporarily interrupted nail formation.
- The lines progress distally with normal nail growth and eventually disappear at the free edge.
- They develop in response to high fevers, scarlet fever, and hand-foot-and-mouth disease, among many other diseases, and in patients taking chemotherapeutic agents.

Digital Mucous Cysts

- Digital mucous cysts are focal collections of mucin lacking a cystic lining.
- These dome-shaped, pink-white structures occur on the dorsal surface of the distal phalanx of middle-aged and elderly people.
- A clear, viscous, jelly-like substance exudes when the cyst is incised.
- Cysts on the proximal nail fold compress the nail matrix cells and induce a longitudinal nail groove.
- Reassurance of the benign diagnosis is usually all that is necessary and most appropriate. Discourage intervention if there is no pain and no compromise of function.
- Cryosurgery of the base may be effective. Remove the cyst roof with scissors and expel the gelatinous contents. Conservatively freeze the base. The treated site becomes edematous and exudative, and a bulla develops in most cases. Healing is complete in 4 to 6 weeks. Retreatment is often necessary.
- High recurrence rates follow surgical excision, intralesional steroid injections, and unroofing of the cyst, followed by electrodesiccation and curettage.

Fig. 20.39 A digital mucous cyst is a clear, shiny papule near the proximal interphalangeal joint.

Fig. 20.40 Digital mucous cyst that has been incised with a #11 blade. Usually it is best just to leave these benign cysts alone rather than try to drain them. Draining may result in infection, and these common benign lesions can recur.

Nevi and Melanoma

- Junctional nevi can appear in the nail matrix and produce a brown-pigmented band. Brown longitudinal bands are common in black people but are rare in white people.
- Forty- to 70-year-olds are at greatest risk.
- Melanoma of the nail can occur anywhere around or under the nail.
- Melanoma of the nail is rare, accounting for <1% of melanomas in white individuals. This is the most common type of melanoma in dark-pigmented persons.
- The lesion may present as a pigmented band that increases in width and is wider at the cuticle end. The pigment tones may be irregular in shading.
- The spontaneous appearance of such a band is noteworthy to most physicians, who promptly require a biopsy.
- Nail plate cracking, distortion, or dystrophy should prompt biopsy. There may be ulceration and bleeding. It is often painless.
- Benign subungual nevi are rare in white people, so subungual nevoid lesions, or red nodules periungually, should be regarded as malignant until proved otherwise.
- Hutchinson's sign is the periungual extension of brown-black pigmentation from longitudinal melanonychia onto the proximal and lateral nail folds. It is an important indicator of subungual melanoma.

Fig. 20.41 A junction nevus appeared in the nail matrix and produced a longitudinal band.

Fig. 20.42 A single linear longitudinal band. A dark nail band on one nail plate deserves further investigation by biopsy because melanoma is in the differential diagnosis.

Fig. 20.43 Multiple nails are affected when medications cause linear nail bands. In this case the offending drug was minocycline. The term for this is longitudinal melanonychia.

Fig. 20.44 Hutchinson's sign. Extension of pigmentation onto the nail folds is a classic sign of subungual melanoma.

Fig. 20.45 Amelanotic melanoma arising in the proximal nail fold region. The erythematous growth has disrupted the normal growth of the nail plate. Growth is usually painless and slow.

Fungal Nail Infections

Description

- Tinea of the nails is a fungal infection of the finger or toenail plate.
- It is caused by many different species of fungi, most commonly *Trichophyton rubrum. Candida* species cause 10% to 20%, and nondermatophyte molds *(Acremonium, Fusarium, Scopulariopsis)* account for a minority of cases.
- When established, it persists. It causes social embarrassment and pain if the nail plate is distorted.

History

- The incidence of fungal nail infections increases with age.
- These infections occur in 15% to 20% of the population between 40 and 60 years of age. In elderly people, the estimated prevalence is 60%.
- They are lifelong; there is no spontaneous remission.
- Trauma from tight-fitting shoes that are too short predisposes to infection. Risk factors include tinea pedis, nail trauma, diabetes, psoriasis, advanced age, peripheral vascular disease, compromised immunity, and personal or family history of onychomycosis.
- A large mass composed of a thick nail plate and underlying debris may cause discomfort with footwear.

Skin Findings

- There are four distinct patterns of nail infection. Several patterns may occur simultaneously in the nail plate.
- Distal subungual onychomycosis is the most common pattern. Fungi invade the distal area of the nail bed. The distal plate turns yellow or white as an accumulation of hyperkeratotic debris causes the nail to rise and separate from the underlying bed.
- White superficial onychomycosis is caused by surface invasion of the nail plate, most often by *Trichophyton mentagrophytes*. The nail surface is soft, dry, and powdery and can easily be scraped away. The nail plate is not thickened and remains adherent to the nail bed.
- In proximal subungual onychomycosis, microorganisms enter the area of the posterior nail fold cuticle and invade the nail plate from below. The surface remains intact. Hyperkeratotic debris causes the nail to separate. *T. rubrum* is the most common cause. This is the most common pattern seen in patients infected with HIV.
- In candidal onychomycosis, nail plate infection caused by *Candida albicans* is seen almost exclusively in chronic mucocutaneous candidiasis—a rare disease. It generally involves all of the fingernails. The nail plate thickens and turns yellow-brown.
- Nail infection may occur with hand or foot tinea or may occur as an isolated phenomenon.
- All nails and the skin are examined to rule out other diseases that mimic onychomycosis.

Fig. 20.46 Distal sublingual onychomycosis is the most common type of fungal nail infection. The fungus invades distally, causing sublingual hyperkeratosis. Infection can be confirmed by a clipping of the nail stained with periodic acid–Schiff stain.

Fig. 20.47 Subungual hyperkeratosis larger than 2 mm is a poor prognostic factor for cure of onychomycosis.

Etiology

- The dermatophytes *T. rubrum* and *T. mentagrophytes* are responsible for most fingernail and toenail infections.
- *Aspergillus, Cephalosporium, Fusarium,* and *Scopulariopsis* species, considered to be contaminants or nonpathogens, can also infect the nail plate.
- Multiple pathogens may be present in a single nail.

Laboratory

- There is a tendency to label any process involving the nail plate as a fungal infection, but many other cutaneous diseases can change the structure of the nail. Some 50% of thick nails are not infected with fungus.
- In a potassium hydroxide wet mount, the subungual debris and nail plate are examined for hyphae. A nail clipping for periodic acid–Schiff (PAS) stain in pathology can confirm diagnosis with good sensitivity.
- The species of fungus is identified before oral antifungal treatment is started. A culture is performed to establish the presence of dermatophytes—organisms susceptible to itraconazole (Sporanox), terbinafine (Lamisil), and fluconazole (Diflucan). Culture can take 4 to 6 weeks.

Fig. 20.48 Subungual onychomycosis. More than 50% of nail involvement is a poor prognostic factor for cure.

- There are no clear guidelines for monitoring patients treated with terbinafine, itraconazole, or fluconazole. A prudent approach would be to order a complete blood count and liver function tests before and 6 weeks into treatment. Laboratory monitoring is not required in patients treated with itraconazole (Sporanox) pulse dosing.
- Histologic study of a nail clipping is performed if the results of the potassium hydroxide examination and culture are

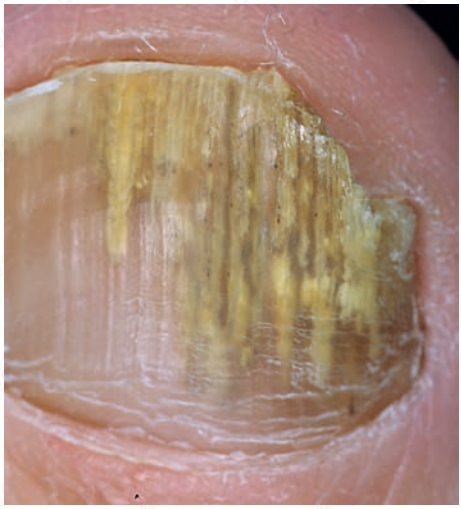

Fig. 20.49 White-yellow or orange-brown streaks are seen in this nail infection and are a poor prognostic sign for cure of onychomycosis.

Box 20.1 Poor Response to Systemic Antifungals

1. Areas of nail involvement >50%
2. Significant lateral disease
3. Subungual hyperkeratosis >2 mm
4. White-yellow or orange-brown streaks in the nail
5. Total dystrophic onychomycosis (with matrix involvement)
6. Nonresponsive organisms (e.g., *Scytalidium* species mold)
7. Patients with immunosuppression
8. Diminished peripheral circulation

negative but clinical suspicion is high. The results of the histologic tests and PAS staining are highly reliable for establishing the diagnosis.

Differential Diagnosis

- Psoriasis is most commonly confused with onychomycosis (the two diseases may coexist). Psoriatic nail disease may present as an isolated phenomenon without other cutaneous signs. The single distinguishing feature of psoriasis—pitting of the nail plate surface—is not a feature of fungal infection
- Leukonychia (the occurrence of white spots or bands that appear proximally and proceed outward with the nail, probably caused by minor trauma)
- Eczema or habitual picking of the proximal nail fold (the nail plate also becomes wavy and ridged)
- Onycholysis (very common in women with long fingernails). It is caused by separation of the nail plate from the nail bed. The yellow or opaque separated nail looks like tinea

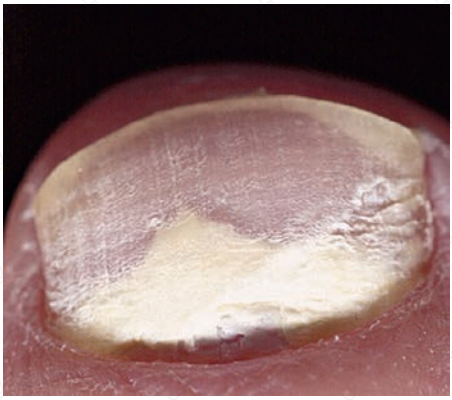

Fig. 20.50 Proximal subungual onychomycosis. Fungal infection of the proximal plate occurs from invasion of fungal hyphae under the proximal nail fold.

Treatment

- Topical antifungal creams are of little value.
- Oral therapy has the highest success rate in fingernail and nail infections in young persons.
- Prolonged use of topical antifungal agents, such as Penlac Nail Lacquer, after clinical response of onychomycosis to an oral agent, may prevent reinfection.
- Systemic therapy is 50% to more than 80% effective. The relapse rate is approximately 15% to 20% in 1 year.
- Choice of systemic therapy must include consideration of drug interactions and comorbidities.
- Indications for treatment include pain with thick nails, functional limitations, secondary bacterial infection, and appearance.
- Terbinafine (Lamisil) 250 mg/day is administered for 6 weeks for infection of the fingernails and 12 weeks for infection of the toenails. Pulse treatment of 250 mg/day for

1 week, then 3 weeks off, repeated once or twice is also an option (54% cure rate if four pulses given). Pulse dosing is not FDA approved. Terbinafine may provide the highest cure rates and longest remission. It is not effective for some candidal species.

- Itraconazole (Sporanox) 200 mg/day is prescribed for 6 weeks for fingernail infection and 12 weeks for toenail infection. The 12-week cure rate is 14%. Pulse dosing with 200 mg twice a day for 1 week on and then 3 weeks off is also an option, and its cure rate is 47% for fingernails. Fingernail infection requires two or three pulses; toenail infection requires three or four pulses.
- Fluconazole is not FDA approved for onychomycosis. Off-label regimens are a single weekly dose of 150 to 450 mg day for 6 months. Efficacy increases with higher dosing.
- Griseofulvin may be effective at very high doses if used for many months, but the other drugs are superior.
- Patients are monitored at 6 weeks and at the end of oral therapy. The infected nail plate is débrided at each visit.
- In most cases, nails do not appear clear at 12 weeks. Patients are reassured that the drug remains in the nail plate for months and will continue to kill fungus.
- Ciclopirox topical solution 0.8% (Penlac Nail Lacquer) has been approved for topical treatment of fingernails and toenails without lunula involvement. Penlac may increase the cure rate when used in combination with systemic antifungal agents.
- Nail clippers with pliers handles may be used to remove substantial amounts of hard, thick debris. The pointed tip of the instrument is inserted as far down as possible between the diseased nail and the nail bed.
- Removing the infected nail plate provides higher cure rates and longer remissions.

Box 20.2 Management of Onychomycosis

1. Confirm the diagnosis (e.g., culture, nail biopsy) before systemic treatment.
2. Identify poor prognostic signs: thick nails, total onychodystrophy, poor perfusion, immunocompromised status, diabetes
3. Débride and trim thick nails.
4. Treat tinea pedis; it is the likely reservoir for relapse.
5. Use antifungal spray or powders in shoes daily.
6. Treat close family contacts.
7. Keep feet cool and dry; wear flip-flops at pools, in locker rooms.
8. Consider occasional pulse or "booster" therapy with a systemic agent to decrease the chance of relapse or reinfection. For example, treat at months 6 and 9 after a traditional 3-month systemic course for recalcitrant toenail disease.
9. Use proper footwear: wide toe box; limited high heels or narrow-toed shoes, which cause micro- or macro-trauma to the normal nail barrier, breaking the seal between the nail plate and nail bed.
10. Trim toenails regularly, cutting straight across and not rounded or in a V-shape at the free margin.
11. Avoid sharing nail clippers and files.

Adapted from Daniel CR III, Jellinek NJ. Commentary: the illusory tinea unguium cure. *J Am Acad Dermatol* 2010;62:415–417.

21 Neonatal Disease

James G. H. Dinulos

Erythema Toxicum Neonatorum

Description

- Erythema toxicum neonatorum is a common benign transient pustular eruption seen in the newborn period.

History

- Erythema toxicum neonatorum occurs more commonly in healthy term infants than in premature and low birth weight infants.
- The cause of erythema toxicum neonatorum is unknown.

Skin Findings

- Erythema toxicum neonatorum lesions appear as "blotchy" macules that develop into superficial pink papules and pustules, taking on a "flea-bitten" appearance.
- Macules can coalesce to form large pink patches studded with only a few to hundreds of pustules.
- Erythema toxicum neonatorum can occur anywhere on the skin, but the face, arms, buttock, and torso are most frequently involved. The palms and soles are rarely affected.
- Overall, erythema toxicum neonatorum can wax and wane with individual lesions appearing to occur in crops. Individual lesions can disappear in hours or last for up to 2 weeks.

Nonskin Findings

- There are no signs of systemic illness.

Laboratory and Biopsy

- A smear (Wright's or Giemsa's stain) of pustule fluid shows abundant eosinophils with relatively few neutrophils.
- For atypical cases, a skin biopsy can be done, showing subcorneal pustules with eosinophils.

Differential Diagnosis

- Bacterial infection (*Staphylococcus aureus,* group B *Streptococcus, Pseudomonas aeruginosa, Listeria monocytogenes, Haemophilus influenzae, Klebsiella pneumoniae*)
- Fungal infection *(Candida)*
- Viral infection (herpes simplex, varicella)
- Transient neonatal pustular melanosis
- Scabies

Course and Prognosis

- Erythema toxicum neonatorum resolves within 3 weeks of life, without any adverse sequelae.

Treatment

- No required treatment.
- Parents should be reassured.

Cutis Marmorata

Description

- Cutis marmorata is a transient benign mottling of the skin that resolves with rewarming.

History

- Cutis marmorata is a common and normal vascular reaction pattern that is seen in both full-term and preterm infants.
- Infants with Down syndrome, trisomy 18, hypothyroidism, neonatal lupus, and septic shock can develop vascular mottling that does not resolve with rewarming.
- Cutis marmorata is thought to be due to an exaggerated vasomotor response to decreased core body temperature.

Skin Findings

- Cutis marmorata manifests as blanching mottled or lace-like erythema that resolves with rewarming.
- It occurs on the trunk and extremities.

Laboratory and Biopsy

- No laboratory testing or biopsy is required.

Differential Diagnosis

- Cutis marmorata telangiectatica congenita is a rare vascular malformation, showing a reticulated vascular pattern with dermal atrophy
- Livedo reticularis is the cutis marmorata–like pattern seen in neonatal lupus

Treatment

- Rewarming results in complete resolution of the erythema.
- Parents should be reassured.

Miliaria

Description

- *Miliaria* is the term describing clear to red papules (miliaria crystallina, miliaria rubra, miliaria profunda) that result from obstruction of the eccrine sweat duct.

History

- Miliaria is very common in newborns and infants who are "bundled" or placed in warm environments.
- In newborns, miliaria crystallina is the most common type and is due to obstruction of the eccrine duct at the level of the stratum corneum. Warming lights and tight bundling can produce miliaria crystallina.
- Miliaria rubra ("prickly heat" or "heat rash") is due to obstruction of the intraepidermal eccrine duct, producing leakage of sweat around the duct, and release of local inflammatory mediators. Miliaria rubra affects infants older than 1 week.
- Miliaria profunda is due to eccrine duct obstruction at the dermal–epidermal junction and is rarely seen in newborns.
- The cause of miliaria is not known, although a polysaccharide produced by certain strains of *Staphylococcus epidermidis* may play a role in obstruction of the eccrine duct.

Skin Findings

- Miliaria crystallina and miliaria rubra show marked involvement of intertriginous areas such as the neck folds. Other common sites include the face (especially the forehead) and trunk.
- Miliaria crystallina is characterized by multiple subtle "dew drop" vesicles. These vesicles are very superficial and break easily with gentle friction.
- Miliaria rubra is characterized by nonfollicular pustules and vesicles.
- Miliaria profunda is characterized by small nonerythematous papules and pustules, occurring on the trunk and extremities.

Nonskin Findings

- Febrile infants are at risk for developing miliaria.

Laboratory and Biopsy

- Generally, skin biopsy is not necessary.

Differential Diagnosis

- Erythema toxicum neonatorum
- Candidiasis
- Insect bites

Course and Prognosis

- Miliaria lasts for hours or days.

Treatment

- No treatment is necessary other than a cool bath and avoidance of tight bundling.

Fig. 21.1 Miliaria crystallina is the most common type of miliaria and is due to obstruction of the eccrine duct at the level of the stratum corneum.

Fig. 21.2 Miliaria rubra ("prickly heat" or "heat rash") is due to obstruction of the intraepidermal eccrine duct, producing leakage of sweat around the duct, and release of local inflammatory mediators.

Fig. 21.3 Erythema toxicum neonatorum. Scattered papules and vesicles on the torso of this 2-week-old infant. Wright stain would show an abundance of eosinophils.

Fig. 21.4 Cutis marmorata telangiectatica congenita. This rare condition may be seen as part of a syndrome, but more commonly it is seen as an isolated deformity. There is a reticular network with atrophy. The atrophy tends to improve with age.

22 Cutaneous Manifestations of Internal Disease

M. Shane Chapman

Acquired Cutaneous Paraneoplastic Syndromes

Description

- Some cutaneous signs are specific enough to warrant a search for occult malignancy.
- Acquired cutaneous paraneoplastic syndromes involve cutaneous findings associated with or related to internal malignancy.
- This chapter will discuss pruritus, dermatomyositis, Sweet's syndrome, carcinoid syndrome, glucagonoma syndrome, paraneoplastic pemphigus, and the sign of Leser–Trélat.

Table 22.1 Cutaneous Lesions and Internal Malignancy: Paraneoplastic Syndromes*

Syndrome	Clinical Presentation	Malignancy
Bazex's syndrome (acrokeratosis paraneoplastica)	Three stages: (1) psoriasiform lesions, tips of fingers and toes; (2) keratoderma, hands and feet; (3) lesions extend locally and new lesions appear on knees, legs, thighs, arms	Carcinoma of esophagus, tongue, lower lip, upper lobes of the lungs
Erythema gyratum repens	Rapidly moving waxy bands of erythema with serpiginous outline and wood-grain pattern	Breast, lung, stomach, bladder, prostate cancer Transitional cell carcinoma of the kidney
Florid cutaneous papillomatosis	Pruritic papules indistinguishable from common viral warts. Lesions first appear on the dorsal aspects of the hands and wrists and then spread to the trunk and occasionally to the face.	Gastric adenocarcinoma and other intra-abdominal cancers Cancers of the breasts, lungs, lymph nodes
Hypertrichosis lanuginosa acquisita (acquired)	Lanugo-type (i.e., fetal) hair (malignant down) near eyebrows and on forehead, ears, nose. Some patients have extensive involvement; hair is easily pulled out.	Solid tumors of the lung (both small cell and non–small cell cancers), colorectal tumors, breast malignancies
Ichthyosis (acquired)	Generalized scaling, rhomboidal scales, prominent on trunk and extremities, spares the flexural area	Hodgkin's disease; other lymphoproliferative malignancies; cancer of lung, breast, cervix
Multicentric reticulohistiocytosis	Reddish-brown papular skin lesions in association with progressive development of severe destructive arthritis. Lesions on face, hands, ears, and forearms. About 50% have oral mucosal involvement.	One third of cases associated with malignancy. Cancers of breasts, lungs, muscles, gastrointestinal and genitourinary tracts, and hematologic system
Palmoplantar keratoderma (tylosis)	Skin thickening of palms and soles. Leads to irregular, cobblestone appearance of the skin	Breast, lung, gastric cancers, leukemias, lymphomas
Peutz–Jeghers syndrome	Pigmented macules on lips and oral mucosa, polyposis of small intestine	Adenocarcinoma of stomach, duodenum, colon
Tripe palms	Rugose, velvety palms. Often occur simultaneously with other paraneoplastic syndromes. Acanthosis nigricans occurs in 75% of cases of tripe palms.	Gastrointestinal and lung malignancies most common Head and neck, genitourinary (ovarian) system

*See text for other examples.

Pruritus

History

- Pruritus is a common symptom of many inflammatory dermatoses.
- In the absence of skin findings, generalized pruritus may indicate occult malignancy.
- Pruritus that is associated with an unknown internal malignancy is more common in gastrointestinal and lymphoproliferative malignancies.

Skin Findings

- Pruritus or itching can be nonspecific and may not be associated with obvious primary skin changes.
- Patients may rub or scratch unknowingly while sleeping and during the examination.
- Scratching may lead to linear edematous changes, hive-like lesions, excoriations, or lichenified or thickened skin.
- Focal areas of hemorrhage or bleeding may be noted.
- Some patients may have generalized scale and xerosis, without other inflammatory changes.
- Pruritus associated with gastrointestinal symptoms, lethargy, weight loss, night sweats, or anemia may alert one to look for malignancy-associated pruritus.

Laboratory and Testing

- Serologic evaluation for liver, biliary, pancreatic, and renal disease are early screening laboratory tests to obtain.
- Routine complete blood count may yield clues to a systemic process or lymphoproliferative disease/bone marrow neoplasia.

Course and Prognosis

- The clinical course and prognosis usually depend on the associated internal malignancy.
- Pruritus may be treated with topical steroids, with or without occlusion and with ultraviolet light phototherapy.
- Systemic therapy with oral steroids can be prescribed but may interfere with the immune system function and malignancy treatment.

Differential Diagnosis

- Generalized pruritus has numerous causes
- Atopic dermatitis, contact dermatitis, psoriasis, scabies, renal disease, liver disease, and lymphoproliferative diseases are a few examples
- All causes must be considered when assessing a patient with an unknown cause of generalized pruritus

Treatment

- Usually, the pruritus improves with treatment of the associated malignancy.
- Antihistamines, topical steroids, emollients (Vaseline), and antipruritic lotions (Sarna) are helpful but not always curative.
- Ultraviolet light phototherapy can be helpful in many patients.
- Systemic therapy with oral steroids can be prescribed but may interfere with the immune system function and malignancy treatment.

Fig. 22.1 Sign of Leser–Trélat (eruptive seborrheic keratosis as a sign of internal malignancy). The sudden appearance of or sudden increase in the number and size of seborrheic keratoses on noninflamed skin has been reported to be a sign of internal malignancy.

Dermatomyositis

History

- Dermatomyositis is a rare skin and muscle disease that can be associated with an underlying malignancy.
- Adults with dermatomyositis are more likely to have an internal malignancy than children.
- The prevalence has been estimated at 5% to 50%, with the greatest prevalence among older patients.
- Some malignancies are diagnosed at the time dermatomyositis is diagnosed.
- The most common associated malignancies are cancers of the ovary, breast, lung, and gastrointestinal tract.

Skin Findings

- The skin findings of dermatomyositis include violaceous papules over the dorsal hand and knuckles (Gottron's papules), periungual telangiectasias, periorbital violaceous or heliotrope coloration, a photosensitive violaceous eruption of the shoulder neck and chest (shawl sign), inflamed scaly palms (mechanic's hands), and diffuse and focal areas of poikiloderma.

Nonskin Findings

- Dermatomyositis may be associated with proximal muscle weakness (polymyositis).
- Some patients with dermatomyositis may have calcification of the muscles.
- Patients with dermatomyositis with signs of internal malignancy, such fever, night sweats, weight loss, without known malignancy, should be carefully evaluated.

Laboratory and Testing

- Skin histology shows an interface dermatitis with increased dermal mucin.
- Serologic evaluation is done for Jo-1 antibodies for dermatomyositis.
- If polymyositis is suspected, a muscle biopsy, electromyographic studies, and creatinine phosphokinase levels should be obtained.
- It is especially important to look for ovarian and breast carcinoma in women.

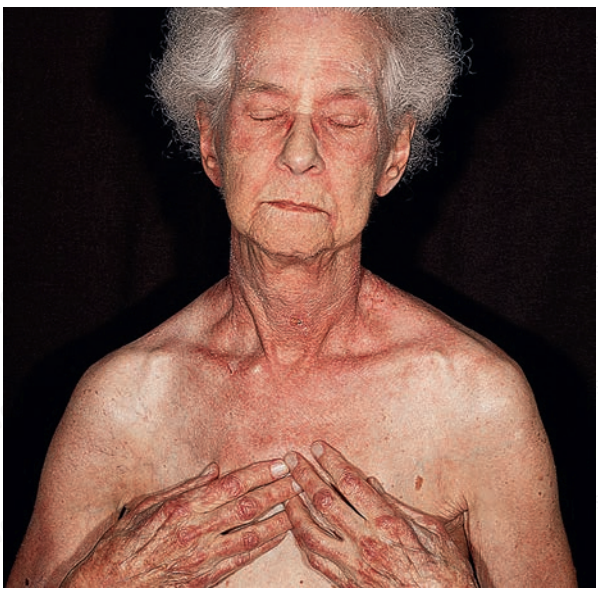

Fig. 22.2 Dermatomyositis. Shown are heliotrope erythema of the eyelids (heliotrope: violet), Gottron's papules (violaceous to red-colored, flat-topped papules that occur over the knuckles and along the sides of the fingers), and a violet erythema that appears on the knuckles and spares the skin over the phalanges and on the sun-exposed areas of the face, neck, back, and arms.

Course and Prognosis

- The clinical course and prognosis usually depend on the associated internal malignancy.
- The signs and symptoms of dermatomyositis may wax and wane, independent of the status of the malignancy, but recurrences or flares of dermatomyositis may indicate a recurrence of the malignancy.
- The risk for malignancy decreases with each subsequent year after the diagnosis of dermatomyositis.

Differential Diagnosis

- Dermatomyositis frequently is confused with lupus, eczematous dermatitis, seborrheic dermatitis, and polymorphous light eruption

Treatment

- Treatment of the malignancy is based on the malignancy type.
- Patients with dermatomyositis should be evaluated first by screening for malignancy.
- Patients with dermatomyositis should avoid intense sun exposure because this can trigger and exacerbate symptoms.
- Some milder cases of dermatomyositis can be treated topically with steroids and emollients.
- Dermatomyositis can be treated with systemic immunosuppressive agents, including systemic steroids, mycophenolate mofetil, cyclosporine, azathioprine, and methotrexate.
- For advanced and more difficult cases, cyclophosphamide and rituximab can be prescribed.

Sweet's Syndrome

History

- Sweet's syndrome is also called acute febrile neutrophilic dermatosis.
- It usually presents as a recurrent, sometimes painful skin eruption associated with fever, elevated white blood cell count, and arthralgias.
- Women are affected more often than men.
- Sweet's syndrome may be associated with acute infection or with lymphoproliferative malignancy.
- Acute myelogenous leukemia is the most common associated malignancy.

Skin Findings

- The lesions of Sweet's syndrome are red, edematous, pseudovesicular, coalescing papules and plaques.
- Lesions vary from 0.5 to 5.0 cm and can be tender on palpation, asymptomatic, or painful.
- Sweet's syndrome lesions are frequently located on the face and dorsal hands, localized or generalized.

Nonskin Findings

- Sweet's syndrome may be associated with an acute infection, in which case there is usually a prodrome of fever and myalgia.
- A generalized nonspecific arthritis can be associated with the syndrome.

Laboratory and Testing

- Histology shows abundant neutrophils in the dermis without vasculitis.

Course and Prognosis

- The clinical course and prognosis usually depend on the associated internal malignancy.
- Malignancy may follow the onset of Sweet's syndrome by 3 months.
- In uncomplicated Sweet's syndrome, lesions tend to resolve in 2 to 3 weeks.

Differential Diagnosis

- Sweet's syndrome can mimic pyoderma gangrenosum, erythema multiforme, bite reactions, lupus, and infections

Treatment

- Sweet's syndrome responds quickly to systemic steroids, but recurrences are common.
- Malignancy and infection should be ruled out before starting steroids.

Fig. 22.3 Sweet's syndrome. Acute tender erythematous plaques, pseudovesicles, and occasionally blisters with an annular or arciform pattern occur on the head, neck, legs, arms, and particularly the back of the hands and fingers. Careful systemic evaluation is indicated, especially when cutaneous lesions are severe or hematologic values are abnormal. Approximately 20% of cases are associated with malignancy.

Fig. 22.4 Sweet's syndrome. Round edematous purulent plaques with central erosions. The dorsal hands are a common location for Sweet's syndrome lesions.

Carcinoid Syndrome

History

- Carcinoid syndrome is an episodic, intense flushing of the face, neck, and upper body.
- It is caused by a neuroendocrine tumor that releases vasoactive mediators (such as serotonin) into the systemic circulation.
- Most carcinoid tumors arise in the small bowel, usually the appendix.
- Usually, vasoactive mediators released from these tumors are inactivated in the liver before reaching the systemic circulation.
- When carcinoid tumors metastasize to the liver, mediators have access to the systemic circulation.
- Carcinoid tumors may also arise in the lung and, as such, release mediators into the systemic circulation.

Skin Findings

- Carcinoid syndrome presents as acute warmth and flushing of the upper body, especially the face, neck, and chest.
- Flushing episodes last for about 30 minutes and are often associated with dyspnea, abdominal cramping, and diarrhea.

Nonskin Findings

- Most carcinoid tumors arise in the small bowel, usually the appendix.
- Usually, vasoactive mediators released from these tumors are inactivated in the liver before reaching the systemic circulation.
- When carcinoid tumors metastasize to the liver, mediators have access to the systemic circulation.
- Carcinoid tumors may also arise in the lung (bronchial) and, as such, release mediators into the systemic circulation.

Laboratory and Tests

- Increased levels of urinary 5-hydroxyindoleacetic acid after 24-hour collection and serotonin elevation in the blood.
- Patients with cutaneous findings suggestive of internal carcinoid malignancy should be carefully evaluated.
- Radiographic testing with computed tomography (CT) or magnetic resonance imaging (MRI) can be used to follow progression of these tumors.

Course and Prognosis

- The clinical course and prognosis usually depend on the size and location of the carcinoid malignancy.

Differential Diagnosis

- Carcinoid syndrome can be confused with rosacea, contact allergy, erysipelas, cellulitis, and pellagra

Treatment

- Treatment is based on the size and location of the carcinoid malignancy at presentation.
- There are not many medical options for treatment of carcinoid tumors, nor prevention for the flushing episodes.
- Surgery is the only effective option for cure, but this is often difficult to achieve.

Glucagonoma Syndrome

History

- A rare, clinically distinctive syndrome consisting of a dynamic generalized cutaneous eruption, necrolytic migratory erythema, associated with a glucagon-secreting tumor of pancreatic alpha cells.

Skin Findings

- Necrolytic migratory erythema describes the eruption of the glucagonoma syndrome.
- It is generalized but favors the flexural areas of the groin, buttocks, and thighs.
- Bright dermal polycyclic patches of erythema evolve into flaccid bullae and desquamate, leaving denuded areas and a collarette of scale.
- The process is dynamic, evolving, and extending each day.

Nonskin Findings

- Glucagonoma syndrome is associated with a tumor of the pancreatic alpha cells.
- Insulin resistance and diabetes mellitus result from increased glucose levels.

Laboratory and Testing

- Necrolytic migratory erythema histology shows a characteristic hydropic degeneration of the superficial epidermis along with intracellular edema.

Course and Prognosis

- The clinical course and prognosis usually depend on the associated glucagonoma.

Differential Diagnosis

- Necrolytic migratory erythema may resemble tinea, candidiasis, eczematous dermatitis, irritant dermatitis, or acrodermatitis enteropathica

Treatment

- Surgical treatment of the glucagonoma tumor is required.
- Octreotide has been used to inhibit the release of glucagon.
- Resolution of the cutaneous changes of necrolytic migratory erythema occurs with tumor removal.

Fig. 22.5 Glucagonoma syndrome (necrolytic migratory erythema). The dermatitis begins as an erythematous area, progresses to superficial blisters, and gradually spreads ("migrates") with central crusting and then healing, followed by hyperpigmentation 7 to 14 days after the initial erythema.

Paraneoplastic Pemphigus

History

- Paraneoplastic pemphigus is a painful immunologic blistering disorder of the mucosa.
- It represents a sign of internal malignancy, most often lymphoproliferative in nature.
- Chronic lymphocytic leukemia is the most commonly associated malignancy.
- Most patients die of complications of paraneoplastic pemphigus or the underlying malignancy.

Skin Findings

- Paraneoplastic pemphigus presents as ocular inflammation, oral erosions, generalized erythema multiforme–like bullous lesions, and denuded areas of skin with crusting.

Nonskin Findings

- Paraneoplastic pemphigus is often associated with a lymphoproliferative or hematologic malignancy.
- Chronic lymphocytic leukemia, non-Hodgkin's lymphoma, and Castleman's disease are the most common malignant associations.

Laboratory

- Skin biopsy shows suprabasilar acantholysis similar to pemphigus vulgaris.
- Antibodies targeted to proteins on the keratinocytes and at the dermoepidermal junction can be found in the skin (direct immunofluorescence) and serum (indirect immunofluorescence).
- Serum antibodies directed against desmoglien 1 and 3, desmoplakin, envoplakin, and periplakin.

Course and Prognosis

- The clinical course and prognosis usually depend on the associated internal malignancy.

Differential Diagnosis

- Paraneoplastic pemphigus mimics other blistering disorders, such as pemphigus vulgaris and mucositis due to chemotherapy

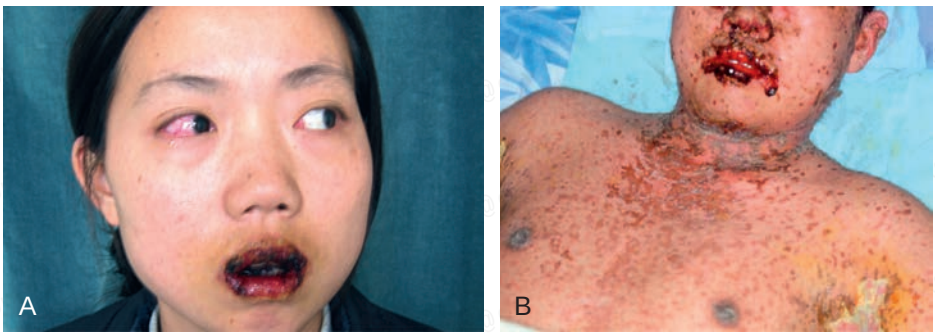

Fig. 22.6 Paraneoplastic pemphigus. **A, B,** Conjunctival reactions and polymorphous skin lesions on the body are the prominent features. (Courtesy of Professor Xuejun Zhu, MD, Department of Dermatology, Peking University First Hospital.)

Sign of Leser–Trélat

History

- The sudden eruptive appearance of numerous seborrheic keratoses may indicate internal malignancy.
- This exceedingly rare and ominous entity is known as the sign of Leser–Trélat.
- Adenocarcinoma of the gastrointestinal tract is the most common associated type of malignancy.

Skin Findings

- Widespread seborrheic keratoses are seen in the sign of Leser–Trélat. Lesions are small, monomorphic, and widespread.

Laboratory and Testing

- The histology of seborrheic keratoses in the sign of Leser–Trélat is similar to that of other inflamed seborrheic keratoses.

Course and Prognosis

- The clinical course and prognosis usually depend on the associated internal malignancy.
- The most common malignancies are adenocarcinomas of the stomach, liver, pancreas, and colorectal tissue.
- Other less common associated cancers are of the breast, lung, and urinary tract.

Differential Diagnosis

- Widespread seborrheic keratosis that are not associated with malignancy
- Eczematous dermatitis, scabies, and other inflamed seborrheic keratoses

Treatment

- The underlying malignancy is treated.
- Inflamed keratosis can be removed with cryotherapy or light electrodesiccation and curettage.

Pearls

- The importance of recognizing the cutaneous findings associated with internal malignancy lies in the fact that the earliest possible detection of tumor usually offers the best prognosis.

Fig. 22.7 A paraneoplastic syndrome; the Leser–Trélat sign. The rapid onset of numerous seborrheic keratoses can be associated with an internal malignancy.

Inherited Cutaneous Paraneoplastic Syndromes

Description

- Inherited cutaneous paraneoplastic syndromes involve cutaneous findings associated with heritable or genetically related conditions that carry an increased risk for internal malignancy.
- This chapter will discuss Cowden's syndrome, Gardner's syndrome, and Muir–Torre syndrome.

History

- A variety of cutaneous lesions may be associated with internal malignancy.
- Recognition of such signs is only of value if it leads to the prevention, early detection, or treatment of internal malignancy.
- Several genodermatoses carry an increased risk for malignancy.
- Patients with such an inherited disorder may benefit from increased surveillance.
- Genetic testing and counseling may be important to patients and their families.

Table 22.2 Some Familial Cancer Syndromes With Cutaneous Findings

Presenting Cancer	Skin Lesion	Syndrome
Colorectal	Sebaceous carcinoma or adenoma, keratoacanthoma	Muir–Torre phenotype of HNPCC
Bowel polyps	Mucocutaneous pigmentation	Peutz–Jeghers syndrome
Colorectal cancer with polyps	Epidermoid cysts, fibromas, lipomas, pilomatricomas	Familial adenomatous polyposis (Gardner's syndrome)
Renal cancer (chromophobe renal cell cancer, hybrid chromophobe oncocytomas)	Triad of lesions including fibrofolliculomas, trichodiscomas, and acrochordons	Birt–Hogg–Dubé syndrome
Renal cell carcinoma (type II papillary renal cancer)	Cutaneous leiomyomas	Hereditary leiomyomatosis, renal cell carcinoma
Prolactinoma	Angiofibromas, collagenomas, café-au-lait macules, subcutaneous lipoma	Multiple endocrine neoplasia type 1
Medullary thyroid cancer, pheochromocytoma, primary parathyroid hyperplasia	Cutaneous lichen amyloidosis	Multiple endocrine neoplasia type 2A
Medullary thyroid cancer, pheochromocytoma	Pedunculated nodules, mucosal neuromas, corneal neuromas, flushing	Multiple endocrine neoplasia type 2B (Wagenmann–Froboese syndrome)
Breast cancer, follicular thyroid cancer, endometrial cancer	Facial trichilemmomas, acral keratosis, papillomatosis of oral mucosa	Cowden's syndrome (*PTEN* hamartoma tumor syndrome)
Basal cell carcinoma	Acrochordons, palmar/plantar pits, epidermal cysts, nevi	Nevoid basal cell carcinoma syndrome (Gorlin's syndrome)

Adapted from Winship IM, Dudding TE. Lessons from the skin: cutaneous features of familial cancer. *Lancet Oncol* 2008;9(5):462–472.

Cowden's Syndrome

Description

- Cowden's syndrome—or multiple hamartoma syndrome—is a rare, autosomal dominant disorder, affecting multiple organ systems.
- Affected people will develop benign and malignant tumors, skin lesions, and tumors of other organs.
- Ductal carcinoma of the breast occurs in more than 30% of female patients with Cowden's syndrome.
- Thyroid and uterine carcinomas are also increased.
- The trichilemmoma is the characteristic cutaneous finding.

Skin Findings

- In Cowden's syndrome, a characteristic variety of facial and oral papules develop during early adulthood.
- The most characteristic facial papule is the trichilemmoma.
- Trichilemmomas are 1- to 3-mm, smooth, and skin colored, and are concentrated around the eyes, nose, malar cheeks, and mouth.
- The oral mucosal papules are 1 mm, smooth, and white, coalescing into a cobblestone pattern on the tongue and gingiva.
- Punctate keratoses of the palms and soles occur in roughly half of patients.

Nonskin Findings

- A variety of benign and malignant neoplasms have been reported in Cowden's syndrome.
- Macrocephaly and hypertelorism are commonly seen in Cowden's syndrome.
- Females have a significantly increased risk for ductal carcinoma of the breast.
- Cerebellar hamartomas (Lhermitte–Duclos disease) are also found in conjunction with Cowden's syndrome.

Laboratory and Testing

- Skin histology of the trichilemmoma shows a symmetric papule with glycogenated clear cells with peripheral palisading and a broad connection with the overlying epithelium.
- The syndrome is now known to be due to a mutation of the tumor suppressor gene *PTEN.*
- Other somewhat related syndromes, including Bannayan–Riley–Ruvalcaba syndrome and Lhermitte–Duclos disease, also have the *PTEN* mutation and seem to have many overlapping features.

Course and Prognosis

- The prognosis depends on the malignancy, the stage at the time of diagnosis, and the treatment.

Treatment

- Screening of family members and genetic counseling are indicated for genodermatoses with an increased risk for malignancy.
- Females suspected of having Cowden's syndrome should have regular breast examinations, mammograms, and very close follow-up.
- Prophylactic bilateral mastectomy has been suggested by some.

Gardner's Syndrome

Description

- Gardner's syndrome is an autosomal dominant condition consisting of multiple epidermal cysts, fibrous tumors of the skin and subcutaneous tissue, and associated intestinal polyposis.
- Malignant degeneration of the intestinal polyps occurs in 50% of patients.
- There is usually a family history of colon cancer.

Skin Findings

- People with Gardner's syndrome develop multiple epidermal cysts, most commonly on the face and scalp.
- Discrete fibrous tumors of the skin are rarely symptomatic.
- The presence of multiple pilar cysts should not be confused with Gardner's syndrome.

Nonskin Findings

- People with Gardner's syndrome develop osteomas of the membranous bones of the head, which are visible on x-ray films.
- Pigmented lesions of the retinal fundus are found in 90% of patients.
- Fundal lesions are usually present in infancy and are useful as a screening finding.
- Supernummary teeth and jaw osteomas are also part of the syndrome.

Laboratory and Testing

- In Gardner's syndrome, histologic testing confirms the scalp cysts as epidermal cysts, rather than pilar cysts.
- Gardner's syndrome is caused by a mutation in the *APC* gene and is considered part of familial adenomatous polyposis.

Course and Prognosis

- The prognosis depends on the malignancy, stage at the time of diagnosis, and treatment.

Treatment

- Screening of family members and genetic counseling are indicated for genodermatoses with an increased risk for malignancy.
- Patients suspected of having Gardner's syndrome should undergo colonoscopy.
- Prophylactic colectomy is usually recommended for patients with Gardner's syndrome.

Fig. 22.8 Cowden's syndrome (multiple hamartoma syndrome). This is an autosomal dominant condition with variable expression. Hamartomas of the skin and mucosa occur in more than 90% of cases. There is an increase in the incidence of breast cancer in women and thyroid cancer in men and women. Other malignancies are reported. Oral mucosal papillomas, seen here, are 1- to 3-mm smooth, white papules. They are present in the gingival, labial, and palatal surfaces of the mouth. Numerous confluent lesions have a cobblestone appearance. Acral keratoses and palmoplantar keratoses are commonly seen.

Muir–Torre Syndrome

Description

- Muir–Torre syndrome is an autosomal dominant condition of multiple benign cutaneous sebaceous tumors and colonic polyps with increased risk for malignant degeneration.

Skin Findings

- Muir–Torre syndrome is suggested by the presence of multiple benign tumors of the sebaceous glands, including sebaceous adenoma, sebaceous epithelioma, and sebaceous carcinoma.
- Of these tumors, the most specific for Muir–Torre is the sebaceous adenoma.
- Patients with Muir–Torre syndrome also develop multiple keratoacanthomas with distinctive sebaceous differentiation.
- Sebaceous hyperplasia is a common condition in otherwise healthy people and is not considered part of the Muir–Torre syndrome.

Nonskin Findings

- A variety of genitourinary malignancies have been described in the Muir–Torre syndrome—all with low incidence.
- The most common malignancy is colon carcinoma, which is usually proximal to the splenic flexure.
- Individuals suspected of having the Muir–Torre syndrome should be screened by colonoscopy.

Laboratory and Testing

- Sebaceous adenoma is the most characteristic lesion of Muir–Torre syndrome.
- Such lesions may have architecture reminiscent of keratoacanthoma.
- The *MLH1* and *MLH2* genes are affected and are involved in a DNA mismatch repair.

Course and Prognosis

- The prognosis depends on the malignancy, the stage at the time of diagnosis, and the treatment.

Treatment

- Patients suspected of having Muir–Torre syndrome should undergo colonoscopy.

Discussion

- Screening of family members and genetic counseling are indicated for genodermatoses with an increased risk for malignancy.
- Patients with genodermatoses may benefit from increased surveillance for likely cutaneous and internal tumors.
- Families of affected people may benefit from screening examination and from genetic counseling.

Pearls

- Patients with multiple trichilemmoma should raise the possibility of Cowden's syndrome.
- A patient with multiple epidermal cysts of the face and scalp should raise suspicion of Gardner's syndrome.
- A skin biopsy showing sebaceous adenoma or keratoacanthoma with sebaceous differentiation should suggest Muir–Torre syndrome.

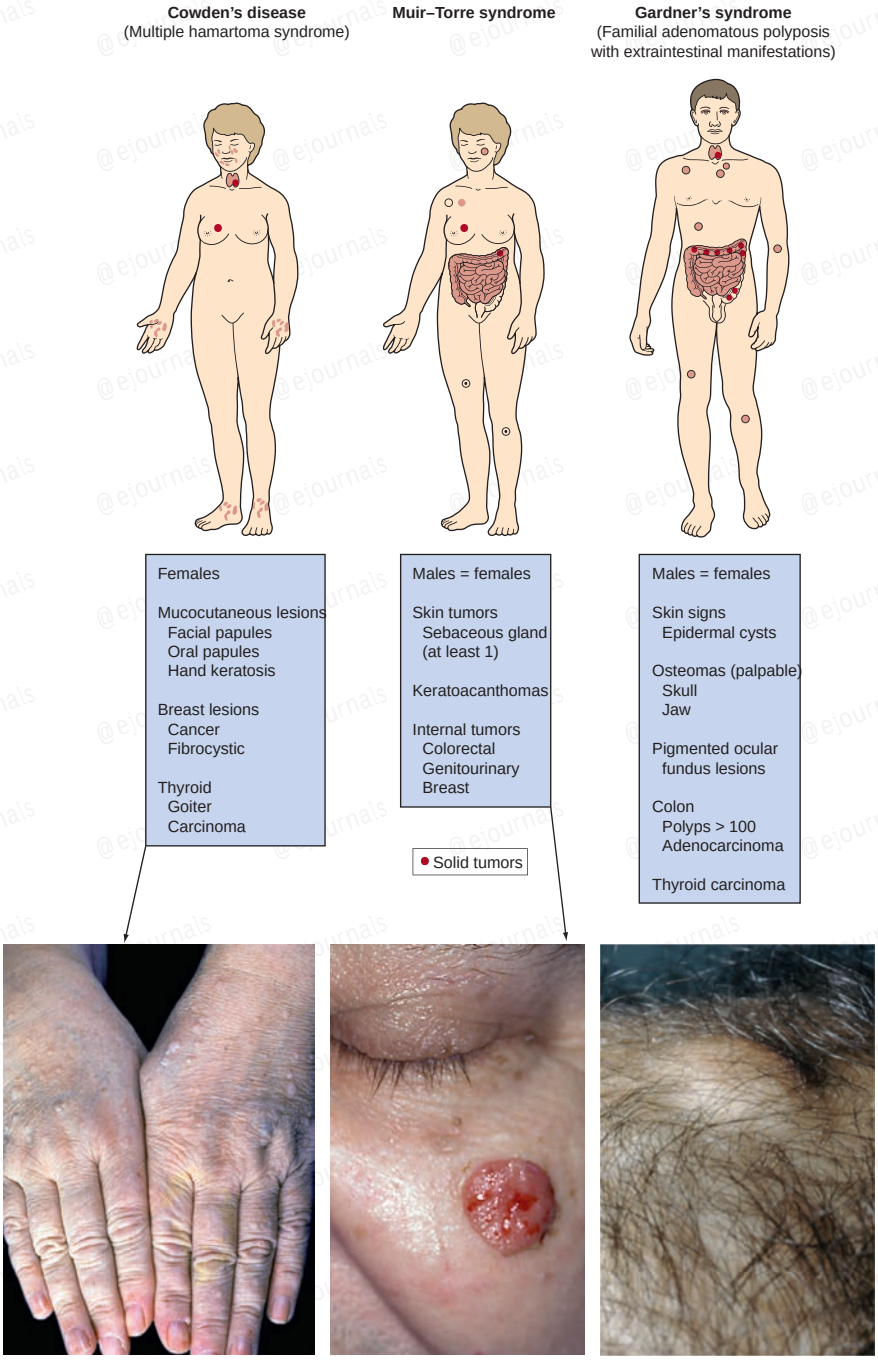

Fig. 22.9 Cowden's disease, Muir–Torre syndrome, and Gardner's syndrome. Each syndrome has several characteristic skin lesions that correspond with the disease, and when the unique skin diagnosis is made, one should consider the associated syndrome.

Acanthosis Nigricans

Description

- Acanthosis nigricans is an elevated, velvety hyperpigmentation of the flexural skin, neck, axillae, and groin.
- It is most commonly associated with obesity, diabetes, and other endocrinopathies.
- It is less commonly associated with medications and occult malignancy.

History

- Patients usually complain of an asymptomatic, dirty appearance to the skin folds that cannot be removed by vigorous washing.
- Usually there is a gradual onset when it is associated with diabetes and obesity.
- Malignancy-associated acanthosis nigricans develops more rapidly and suddenly.
- Attempts to rub, scrub, or remove the skin changes are futile.
- There may be a family history of the eruption.

Skin Findings

- There is a symmetric, velvety brown thickening of the skin.
- The surface is rough, warty, or papillomatous.
- The axillae and neck are most commonly involved.
- The crural folds, belt line, dorsal fingers, umbilicus, mouth, and areolae of the breast may also be involved.
- The severity is variable from mild to extensive.
- Acanthosis nigricans is usually asymptomatic.

Nonskin Findings

- Acanthosis nigricans is a cutaneous marker of tissue insulin resistance.
- Patients without diabetes have high levels of circulating insulin or an impaired response to exogenous insulin.
- The vulva is commonly affected in obese, hirsute, hyperandrogenic, or insulin-resistant women.
- HAIR-AN syndrome is *hyperandrogenism, insulin resistance,* and *acanthosis nigricans.*

Laboratory and Testing

- Glucose levels may be elevated. Other studies are not routinely done.
- There are high levels of circulating insulin.
- There is an impaired response to exogenous insulin.

Discussion

- Acanthosis nigricans can be caused by medications, such as estrogens and nicotinic acid.
- Associated internal malignancies are usually adenocarcinomas of the gastrointestinal tract and uterus.
- Other, less common associated tumors include those of the lung, prostate, breast, and ovary.
- Other endocrinologic disorders, such as pineal gland tumors, are possible etiologies.

Treatment

- The eruption is usually asymptomatic and does not require treatment.
- Reducing thick lesions in areas of maceration may decrease the odor and promote comfort.
- Lactic acid cream 12% or tretinoin cream or gel can be applied to decrease thickness of the skin of acanthosis nigricans.
- There is no treatment that is uniformly effective at completely eradicating the skin changes.

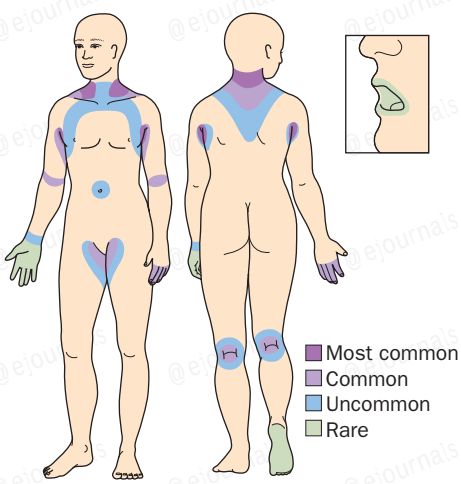

Fig. 22.10 Acanthosis nigricans distribution diagram.

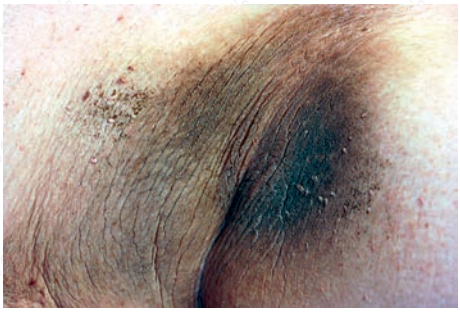

Fig. 22.11 Acanthosis nigricans. Hyperpigmented, elevated, rough "velvety" patches in the axillae, which is a common location for acanthosis nigricans. Other skin folds, especially the posterior neck, can also be involved.

Fig. 22.12 Acanthosis nigricans. The most common site of involvement is the axilla, but the changes may be observed in the flexural areas of the neck and groin, at the belt line, over the dorsal surfaces of the fingers, in the mouth, and around the areolae of the breasts and umbilicus.

Fig. 22.13 Acanthosis nigricans. There is a symmetric, rough, brown thickening on the neck folds extending to the shoulders. In time, the skin can develop a leathery, warty, and papillomatous surface.

Pearls

- The most common areas involved are the axillae and neck.
- Patients who have this during puberty and into adulthood usually have insulin resistance.
- A sudden onset and extensive acanthosis nigricans should prompt an evaluation for internal malignancy, such as stomach adenocarcinoma.

Neurofibromatosis

Description

- Neurofibromatosis is an inherited disorder of the skin and central nervous system made up of at least seven clinical variants.
- Neurofibromatosis type 1 is the most common variant.
- It is also called von Recklinghausen's disease.

History

- The inheritance is autosomal dominant, but 50% of cases arise from a new mutation.
- The incidence is estimated at 1 in 3000. It affects males and females equally.
- The pathogenesis is believed to be a defect in the neurofibromin gene.
- Neurofibromin is a suppressor of products of *ras* proto-oncogenes, and its loss leads to tumor progression.
- Neurofibromatosis is characterized clinically by café-au-lait macules, neurofibromas, axillary and groin freckling, Lisch's nodules in the iris, and body defects.

Skin Findings

- Neurofibromas are pink or flesh-colored, soft, pedunculated papules that may be tender. The number varies from a few to hundreds or thousands.
- Dermal and subcutaneous neurofibromas can be present at about 5 years of age but typically start appearing around puberty and increase in number with age and with pregnancy.
- Café-au-lait macules are randomly distributed, tan to brown patches which increase in number and size in the first 5 years of life; more than six café-au-lait macules greater than 5 mm in diameter suggests the presence of neurofibromatosis type 1.
- Axillary or inguinal freckling (Crowe's sign) is specific for the disease.
- Plexiform neurofibromas occur along the course of peripheral nerves, creating large, tender nodules or poorly demarcated masses, often with overlying hyperpigmentation and hypertrichosis. About 20% of neurofibromatosis patients have plexiform neurofibromas. When present, these tumors are highly diagnostic of neurofibromatosis.
- Malignant degeneration of cutaneous neural tumors occurs in 2% of patients but is rare before the age of 40 years.

Nonskin Findings

- Lisch's nodules are asymptomatic iris hamartomas and occur in more than 90% of neurofibromatosis patients older than 6 years. A slit-lamp examination is needed for Lisch's nodules.
- Optic gliomas occur in two thirds of patients; they are usually asymptomatic but may lead to blindness.
- Other tumors of the central nervous system that are seen with increased frequency include astrocytomas, meningioma, vestibular schwannoma (acoustic neuroma), and ependymomas.
- Patient may have seizures, learning disabilities, poor coordination, and hydrocephalus.
- Noncentral nervous system tumors occurring in neurofibromatosis type 1 include neurofibrosarcoma, rhabdomyosarcoma, pheochromocytoma, and Wilms' tumor.
- Renovascular abnormalities may include renal artery stenosis.
- Skeletal abnormalities include short stature, scoliosis, sphenoid wing dysplasia, and macrocephaly.
- Peer relationships and psychosocial adjustment are often major issues during adolescence.

Laboratory and Testing

- MRI of the brain and spinal cord may show various central nervous system tumors.
- Histologically, neurofibromas are well-circumscribed, unencapsulated aggregations of small nerve fibers and spindle cells, with wavy nuclei in the dermis.
- Genetic testing is available.

Course and Prognosis

- There is great variation in the severity of the disorder.
- Vision and cognitive function may be impaired by central nervous system tumors.
- Central nervous system tumors are usually not present in childhood, but they begin to appear at puberty.

- Tumors increase in both number and size as the patient ages.
- Life-threatening complications may include seizures, increased intracranial pressure, vascular complications from hypertension, and malignancy.

Discussion

- The differential diagnosis includes McCune–Albright syndrome, Noonan's syndrome, and Proteus syndrome.
- Consensus criteria for diagnosis were adopted in 1987 by the National Institutes

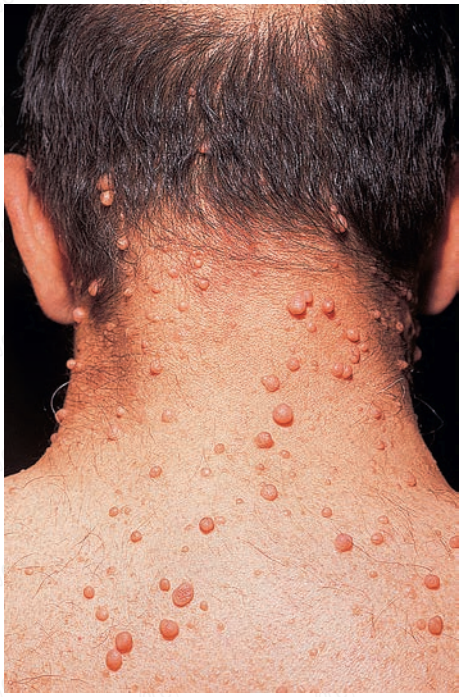

Fig. 22.14 Neurofibromatosis. Tumors are usually not present in childhood, but they begin to appear at puberty. Tumors increase in both number and size as the patient ages.

Fig. 22.15 Neurofibromatosis. The most common tumors are sessile or pedunculated. Early tumors are soft, dome-shaped papules or nodules that have a distinctive violaceous hue. Most are benign.

Fig. 22.16 Neurofibromatosis. Lisch's nodules are pigmented, melanocytic, iris hamartomas. They increase in number with age and are asymptomatic. All adults with neurofibromatosis who are 21 years or older have Lisch's nodules. Slit-lamp examination is essential for differentiation from iris freckles or nevi.

of Health. These criteria require two or more of the following features:
- Six or more café-au-lait macules more than 5 mm in greatest diameter in prepubertal children and more than 15 mm in greatest diameter in postpubertal people.
- Two or more neurofibromas of any type, or one plexiform neurofibroma.
- Freckling in the axillary or inguinal regions.
- Optic glioma.
- Two or more Lisch's nodules.
- A distinctive osseous lesion, such as sphenoid dysplasia, or thinning of long-bone cortex, with or without pseudoarthrosis.
- A first-degree relative (parent or sibling) with neurofibromatosis type 1.

- Lisch's nodules are rare in the general population, so their presence in people older than 6 years—suspected of having neurofibromatosis—is virtually diagnostic.

Treatment

- Care is best performed by a multidisciplinary approach, with regular follow-up by the primary care physician, ophthalmologist, neurologist, and dermatologist.
- Head circumference and blood pressure should be monitored closely in children.
- Hypertension in a child may indicate renal artery stenosis. In an adult, it may suggest pheochromocytoma.
- The patient should be referred to an orthopedist, a psychiatrist, and a neurosurgeon, as indicated.
- First-degree relatives should be screened for cutaneous and ophthalmologic signs of neurofibromatosis.
- Genetic counseling of patients and their families is recommended.
- There is a 50% chance of inheritance with nearly 100% penetrance. Patients who inherit the gene show clinical signs of neurofibromatosis type 1.

Pearls

- An ophthalmologist should perform a slit-lamp examination looking for Lisch's nodules. These lesions are highly specific findings for neurofibromatosis type 1.
- Patients and their families should be encouraged to contact local neurofibromatosis support groups.

Pediatric Considerations

- Definitive diagnosis may not be possible until the pubertal years.
- Café-au-lait macules and neurofibromas are not necessarily diagnostic of neurofibromatosis, unless they are associated with other signs and meet the previously discussed criteria.
- Neuroimaging the asymptomatic neurofibromatosis patient is controversial. Seizures, hypertension, and musculoskeletal changes may warrant radiologic workup early in the disease process.
- Children who have multiple café-au-lait macules, but do not fulfill clinical diagnostic criteria for neurofibromatosis type 1, should have the following annual examinations:
  - Eye examination in first decade of life (looking for optic gliomas).
  - Developmental assessment.
  - Scoliosis monitoring.
  - Complete neurologic examination.
  - Blood pressure screening.

Fig. 22.17 Café-au-lait spots are the earliest manifestation of neurofibromatosis. The brown macules can appear in infancy. They enlarge in size after age 2 years. They show marked variation in size. Some have smooth borders; others are irregular. Patients may have café-au-lait spots as an isolated finding. They are also found in tuberous sclerosis, Fanconi's anemia, and McCune–Albright syndrome.

Fig. 22.18 Von Recklinghausen's neurofibromatosis. Axillary freckling (Crowe's sign) is a pathognomonic sign.

Tuberous Sclerosis

Description

- Tuberous sclerosis or tuberous sclerosis complex is an uncommon genodermatosis affecting the skin and central nervous system, as well as multiple other organs.
- Tuberous sclerosis is also called Bourneville's disease and epiloia.
- It is caused by mutations of the *TSC1* gene that encodes the protein, harmartin, and the *TSC2* gene that encodes tuberin.
- These two genes are tumor growth suppressor genes regulating cell growth and differentiation, but when mutated allow multiple types of tumors in multiple organs to proliferate.

History

- The incidence is estimated at 1 in 10,000, with an equal male and female distribution.
- Spontaneous mutations account for 75% of cases and autosomal dominant transmission for the other 25%.
- A "two-hit hypothesis" has been proposed to explain the variability of tuberous sclerosis.

Skin Findings

- The disorder typically presents at or just after birth.
- The earliest sign is "ash-leaf" hypopigmented macules, usually found on the trunk or extremities.
- Hypopigmented macules are also found in 0.2% to 0.3% of normal neonates but are present in at least half of those with tuberous sclerosis.
- Polygonal, hypopigmented "confetti" macules are also common, especially in the pretibial area.
- Wood's light examination accentuates the appearance of ash-leaf macules.
- Facial angiofibromas, also named *adenoma sebaceum,* appear in early childhood and increase in number throughout adolescence. These benign hamartomas are smooth, firm, pink papules measuring 1 to 5 mm that appear on the nasolabial folds, cheeks, and chin.
- The shagreen patch is a connective tissue nevus seen in roughly 80% of patients with tuberous sclerosis. Typically located in the lumbosacral area, the shagreen patch is a 1- to 5-cm, white to yellow plaque with a pebbled surface.
- Periungual fibromas or Koenen's tumors are conical, pink, firm projections from the posterior nail folds of the fingers and toes. They appear around the time of puberty and persist indefinitely. Histologically, these are angiofibromas.
- Fibrous, flesh-colored, discrete plaques on the forehead are sometimes seen and, if present, are considered to be virtually pathognomonic of tuberous sclerosis.

Nonskin Findings

Central Nervous System

- Cortical tubers consisting of astrocytes and giant cells, paraventricular calcification, subependymal hamartomas, and astrocytomas may be seen on imaging studies of the head.
- Seizures occur in 75% of patients with central nervous system lesions.
- Infantile spasms and intellectual disability are also part of the syndrome.
- About half of patients with tuberous sclerosis have learning difficulties.

Renal System

- Angiomyolipoma of the kidneys are seen in more than 60% of tuberous sclerosis patients and may present with hematuria.
- Multiple renal cysts are present in 20% to 30% of tuberous sclerosis patients, which can be associated with polycystic kidney disease and lead to renal failure.

Cardiac System

- Cardiac rhabdomyomas are benign striated muscle tumors found in 50% of tuberous sclerosis patients, identified on echocardiogram.
- These tumors grow in utero, may be visible in the second half of pregnancy, and then completely regress in some cases.
- Patients may present with arrhythmias and murmurs.

Pulmonary System

- Pulmonary cysts, similar to lymphangioleiomyomatosis, may be seen on

chest radiographs and may occasionally result in spontaneous pneumothorax.

Other Organ Systems

- Retinal hamartomas (phakomas), gray or white patches, may be seen on funduscopic examination.
- Careful examination of the oral cavity may reveal enamel pits and gingival fibromas.
- Phalangeal cysts and periosteal thickening may be seen on plain films of the hands.

Laboratory and Testing

- Skin histology of the facial angiofibromas (adenoma sebaceum) is consistent with angiofibromas.
- Skin histology of ash-leaf macules shows the presence of melanocytes but a decrease in melanin, which is different from vitiligo, in which all melanocytes are destroyed.
- Histology of a shagreen patch shows an increased number of collagen bundles, which is consistent with connective tissue nevus.
- Transfontanel ultrasound, CT, and MRI may demonstrate both benign and malignant central nervous system lesions.
- An electroencephalogram may reveal areas of seizure activity.
- An echocardiogram can show rhabdomyomas, angiolipomas, and renal cysts.
- Funduscopic examination confirms the presence of retinal hamartomas.
- Renal ultrasound and echocardiogram should be performed in pregnant woman and neonates when the diagnosis of tuberous sclerosis is suspected.
- Genetic testing can be performed looking for deletion mutations in *TSC1* on chromosome 9 and *TSC2* on chromosome 16.

Course and Prognosis

- About 40% of affected people have normal intelligence; the remainder have subtle or mild intellectual disability.
- Cutaneous manifestations may not correlate with mental ability.
- Premature death occurs rarely, most often from status epilepticus or malignant brain tumor.

Differential Diagnosis

- Hypopigmented macules
- Vitiligo, nevus anemicus, hypomelanosis of Ito, idiopathic guttate hypomelanosis

Fig. 22.19 Adenoma sebaceum is the most common cutaneous manifestation of tuberous sclerosis. The lesions consist of smooth and firm 1- to 5-mm, yellow-pink papules with fine telangiectasia.

Fig. 22.20 Adenoma sebaceum. The angiofibromas are located on the nasolabial folds, cheeks, and chin and occasionally the forehead, scalp, and ears. The number varies from a few inconspicuous lesions to dense clusters of papules. They are rare at birth but may begin to appear by ages 2 to 3 years and proliferate during puberty.

Fig. 22.21 The shagreen patch. There is usually one lesion, but several may be present. They are soft, flesh-colored to yellow plaques with an irregular surface that has been likened to pig skin. The lesion consists of dermal connective tissue and appears most commonly in the lumbosacral region.

- Shagreen patch
- Congenital nevus, other types of hamartomas
- Adenoma sebaceum
- Acne, Cowden's syndrome, multiple endocrine neoplasia, multiple trichoepitheliomas, Birt–Hogg–Dubé syndrome

Treatment

- Complete physical examination with routine follow-up by the primary care physician.
- Imaging studies should be performed to look for cardiac, renal, and central nervous system tumors.
- Referral to a pediatric neurologist, including continued long-term follow-up, should be considered for seizure management.
- Baseline ophthalmologic evaluation should be performed.
- Carbon dioxide laser ablation or shallow shave removal of facial angiofibromas can significantly improve the cosmetic appearance and self-image.
- If needed, special educational planning should help the patient reach maximal potential.
- Careful cutaneous and general examination of first-degree relatives, as well as genetic counseling, is recommended.
- There is currently no genetic or medical treatment, but rapamycin has been shown to improve learning in animal models.

Pediatric Considerations

- Adenoma sebaceum lesions or facial angiofibromas are common in tuberous sclerosis patients and may be misdiagnosed as acne. Cosmetic removal may be indicated.
- Hypomelanotic macules are the earliest sign of tuberous sclerosis and can be missed unless examined with a Wood's lamp.
- Imaging studies of the cranium should be obtained after the diagnosis is confirmed to look for subependymal nodules. These may be difficult to distinguish from astrocytomas.
- Local and national support groups (e.g., Tuberous Sclerosis Alliance at http://www.tsalliance.org) can be valuable sources of information and comfort to affected families.

Fig. 22.22 Tuberous sclerosis. Hypomelanotic macules (oval or ash-leaf shaped, stippled, or confetti-like) are randomly distributed with a concentration on the arms, legs, and trunk. They are the earliest sign of tuberous sclerosis.

Fig. 22.23 Tuberous sclerosis. Multiple periungual fibromas of the fingers and toes are characteristic of tuberous sclerosis.

Granuloma Annulare

Description

- Granuloma annulare is a slowly progressive, self-limited, granulomatous-like dermal skin disease.
- It is characterized by round or annular plaques that may initially resemble tinea and spontaneously disappear and recur over time.
- There is a localized form, rare generalized form, and even more uncommon subcutaneous variant.

History

- The female-to-male ratio is 2:1.
- The duration of each lesion is highly variable. Most lesions resolve without medical intervention.
- About 70% of patients are younger than 30 years, and 40% are younger than 15 years.
- About 50% of patients are clear in 2 years, but 40% experience recurrence in the same site.
- Lesions tend to be asymptomatic.
- Patients become concerned when multiple lesions in multiple areas develop and expand.

Skin Findings

- The disease begins with an asymptomatic, flesh-colored papule that undergoes central involution.
- Small, firm, flesh-colored or violaceous papules may then evolve into a ring-like plaque.
- Eventually, a concentric annular plaque develops that may slowly increase in diameter, up to 1 to 5 cm.
- The localized form is usually found on the lateral or dorsal surfaces of the hands and feet and on the extensor aspects of the arms and legs.
- Individual lesions may persist for many years, then vanish, only to appear later in life at the same or different locations.
- Disseminated or generalized granuloma annulare occurs in adults and appears with numerous flesh-colored or violaceous papules, some of which form annular rings. The papules may be accentuated in sun-exposed areas. The course is variable but may persist for many years.

Nonskin Findings

- The association of granuloma annulare with diabetes mellitus is controversial.
- Most patients with the localized form do not have clinical or laboratory evidence of diabetes.
- The association between disseminated granuloma annulare and diabetes has been established, but the frequency is unknown.

Laboratory and Testing

- The clinical presentation is characteristic, and biopsy may not be required.
- Histologic testing shows characteristic collagen degeneration, chronic inflammation, and fibrosis.
- A potassium hydroxide examination may be performed to rule out tinea.

Differential Diagnosis

- Tinea
- Necrobiosis lipoidica
- Nummular eczema

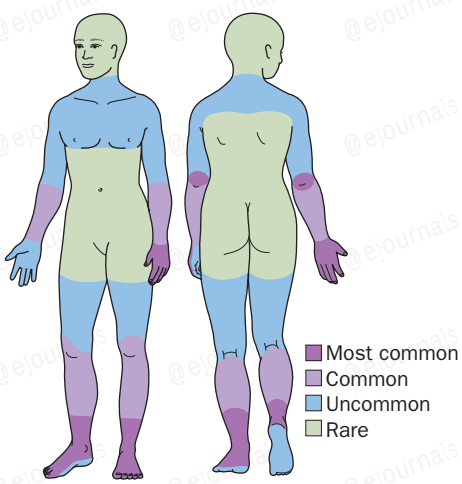

Fig. 22.24 Granuloma annulare distribution diagram.

Fig. 22.25 The plaques of granuloma annulare show a red-brown to violaceous color, with a sharp, elevated border and slight hypopigmentation centrally. The dorsal hands and dorsal feet are common locations. Granuloma annulare can be easily confused with tinea.

Fig. 22.26 Granuloma annulare. The borders are elevated with confluent papules. Patients might think they have "ring worm." The eruption extends peripherally for months and usually resolves spontaneously in 2 to 3 years.

Fig. 22.27 Granuloma annulare. The disease begins with an asymptomatic flesh-colored papule that undergoes central involution. The ankle is a common site.

Fig. 22.28 Granuloma annulare. This lesion was dense enough to restrict range of motion of the finger.

Treatment

- Localized lesions are asymptomatic and are usually left untreated.
- Superpotent topical steroids used daily at intervals of 2 to 3 weeks are sometimes effective.
- Lower-potency topical steroids can be occluded for shorter periods of time.
- Intralesional triamcinolone acetonide 2.5 to 5 mg/mL should be injected only into the elevated border. This is predictably effective and induces long periods of remission. Local atrophy is the potential side effect.
- Disseminated granuloma annulare has been reported occasionally to respond to dapsone 100 to 200 mg daily and to isotretinoin, hydroxychloroquine, and niacinamide 1.5 g daily.

Fig. 22.29 Granuloma annulare. These plaques have been present for months. The borders are elevated with central clearing. A biopsy at the inflamed elevated edge of the annular plaque confirmed the diagnosis of granuloma annulare. This is an unusual variant of granuloma annulare.

Pearls

- Granuloma annulare is often initially diagnosed as tinea because of the round tinea-like pattern.
- The border of granuloma annulare does not scale, whereas the border of tinea usually does.
- Unlike necrobiosis lipoidica, granuloma annulare is associated with diabetes.

Fig. 22.30 Granuloma annulare is characterized by a ring of small, firm, flesh-colored or red papules.

Fig. 22.31 The ankle is a common site to find granuloma annulare.

Necrobiosis Lipoidica

Description

- Necrobiosis lipoidica is an inflammatory condition characterized by collagen degeneration.
- When present, necrobiosis lipoidica is often associated with diabetes; therefore, it is called necrobiosis lipoidica diabeticorum.
- However, only 1% of patients with diabetes develop necrobiosis lipoidica.

History

- More than 50% of people with necrobiosis lipoidica also have insulin-dependent diabetes.
- Lesions may appear years before the onset of diabetes.
- Lesions usually develop slowly and are often asymptomatic initially.
- The onset may occur at any age, but the disease most commonly starts in the third and fourth decades.
- About 75% of those affected are women.

Skin Findings

- Lesions are usually limited to the anterior shins but may be seen on the calves, thighs, arms, hands, feet, and scalp.
- They begin as round, violaceous patches and slowly expand.
- The advancing border is red, and the central lesion turns a characteristic orange-yellow to brown.
- The central area atrophies and shows a shiny, waxy surface with prominent telangiectasias.
- Ulceration may occur, particularly after trauma, in about 15% of cases. These ulcers can be exquisitely tender and very difficult to heal.

Nonskin Findings

- The term necrobiosis lipoidica diabeticorum for all cases has fallen out of favor because a significant minority of affected people do not have diabetes; therefore, necrobiosis lipoidica may be more appropriate.

Laboratory and Testing

- Clinical features are often so characteristic that biopsy is not required, although in some cases biopsy can be helpful.
- In general, the location and the lesion itself heal poorly, so biopsy risks and healing challenges must be weighed.
- Because necrobiosis lipoidica diabeticorum may be the presenting sign of diabetes, a glucose tolerance test or hemoglobin A1C level may be considered.

Course and Prognosis

- The course of necrobiosis lipoidica diabeticorum is unpredictable.
- The number or severity of lesions or ulcerations has not been correlated with the degree of diabetic control.
- Lesions usually heal with atrophic scarring but can be chronic and recurrent.

Treatment

- Topical and intralesional steroids arrest inflammation but may promote further atrophy.
- Mid- to high-potency corticosteroids can be used under occlusion for short periods.
- A short course of oral corticosteroids can be considered if disease activity and symptoms are severe, but this is rarely the case.
- Pentoxifylline can be helpful in some patients and has been used in combination

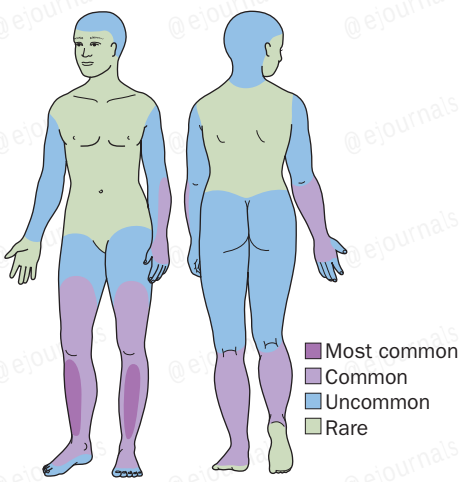

Fig. 22.32 Necrobiosis lipoidica distribution diagram.

with low-dose aspirin for ulcerating necrobiosis lipoidica.
- Skin grafting can be effective for extensive disease, but graft survival is not guaranteed.
- Conservative, minimal care may be the best approach.

Pearls

- Patients with necrobiosis lipoidica, without overt diabetes, should be evaluated periodically for the development of new-onset diabetes.

Fig. 22.33 Necrobiosis lipoidica. The eruption begins as an oval violaceous patch and expands slowly. The advancing border is red, and the central area turns yellow-brown. The central area atrophies and has a waxy surface. Telangiectasias become prominent.

Fig. 22.34 Necrobiosis lipoidica. More than 50% of patients with this condition are generally insulin dependent. Most are females, and in most cases the lesions are confined to the anterior surfaces of the lower legs.

Fig. 22.35 Necrobiosis lipoidica. Chronic inflammation and ulceration healed with bound-down scars. Treatment with intralesional corticosteroids helped to control the disease activity.

Fig. 22.36 Large plaques of expanding necrobiosis lipoidica lesions, with the characteristic atrophic yellow-orange center, early erosion, and ulceration.

Pyoderma Gangrenosum

Description

- Pyoderma gangrenosum is an inflammatory, necrotizing, noninfectious, ulcerative skin disease characterized by a rapidly enlarging, ulcerative lesions, usually on the legs.

History

- Lesions may begin spontaneously or at the site of trauma.
- Most cases occur in people aged between 25 and 55 years.
- Pyoderma gangrenosum is rare in children.
- The disease is commonly associated with inflammatory bowel disease, Crohn's disease, ulcerative colitis, and rheumatoid arthritis.
- Less commonly, it is associated with chronic active hepatitis, a monoclonal gammopathy, myelodysplasia, paraproteinemia, myeloid leukemias, multiple myeloma, and various solid tumors.
- Pathergy (enlargement of the lesion) with trauma is a characteristic of pyoderma gangrenosum.
- Postsurgical pyoderma gangrenosum may masquerade as wound dehiscence or infection.

Skin Findings

- Pyoderma gangrenosum classically presents as a painful ulcer with a rolled or undermined border.
- The most common sites are the lower legs, buttocks, and abdomen.
- It is rare to see pyoderma gangrenosum on the upper body or face, but this can occur.
- The initial lesion begins as a tender, inflamed red or dusky macule, papule, pustule, nodule, or bulla.
- It is often described as a pustule or inflamed red nodule that ulcerates, forming a painful, sharply marginated, violaceous bordered ulcer with a purulent or fibrinous base.
- The edge of the ulcer is characteristically rolled or elevated (undermined) and inflamed.
- The ulcer may have tiny pustules along the border.
- Expansion of the ulceration can occur rapidly, over just a few days.
- The fully evolved, classic ulcerated lesion is generally 3 to 10 cm.
- Multiple lesions are usually present.
- Eventually, smaller lesions may coalesce into larger ulcers with crater-like holes and small fistula tracks.
- Lesions gradually heal, with irregular, cribriform, or stellate scarring.
- Historically, pyoderma gangrenosum is divided into four variants—pustular, bullous, ulcerative, and vegetative forms—but each of these types may coexist in the same patient, and one lesion may evolve from one variant to another.

Nonskin Findings

- Pyoderma gangrenosum can be associated with inflammatory bowel disease, ulcerative colitis, and Crohn's disease, in about 30% of cases.
- Patients with pyoderma gangrenosum, without a history of inflammatory bowel disease and with no gastrointestinal symptoms, may still have inflammatory bowel changes on colonoscopy.
- Arthritis, multiple myeloma, and other gammopathies may also accompany pyoderma gangrenosum.
- Most cases of an internal malignancy–associated pyoderma gangrenosum are due to a known cancer, but one should look for internal malignancy if not initially evident.

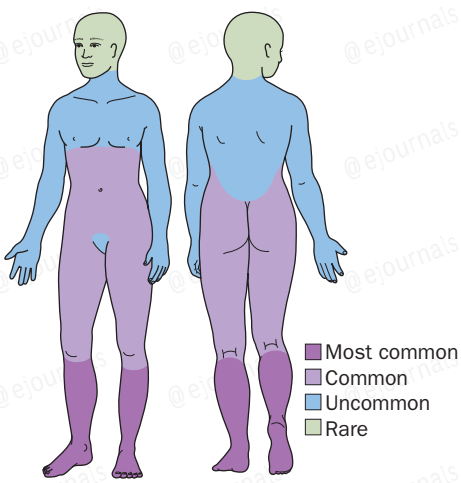

Fig. 22.37 Pyoderma gangrenosum distribution diagram.

Laboratory and Testing

- The histology of pyoderma gangrenosum is not always diagnostic.
- There are characteristic changes, such as hemorrhage, necrosis, vasculitis, and coagulation, at the advancing border. There is a massive inflammatory cell infiltrate with neutrophils and other cell types. Therefore, pyoderma gangrenosum is considered to be one of the neutrophilic dermatoses.
- Colonoscopy can be requested to look for associated inflammatory bowel disease, even in the absence of symptoms.
- Serum protein electrophoresis may identify an underlying gammopathy.
- Associated conditions should be sought and infections excluded.

Differential Diagnosis

- Sweet's syndrome, systemic vasculitis, Behçet's disease, spider bite, and infection

Treatment

Systemic Therapy

- Hospitalization may be necessary for severe cases. Analgesia and systemic therapy are often required.
- Most patients require combination therapy with multiple systemic immunosuppressants to reduce recurrence and resolve the inflammation.
- High-dose systemic oral steroids or intravenous steroids should be administered initially to try to quickly suppress the immune response in the short term.
- Cyclosporine is also an effective nonsteroidal immunosuppressant for pyoderma gangrenosum and can be used in combination with systemic steroids in appropriate patients.
- Mycofenolate mofetil, dapsone, minocycline, clofazimine, and thalidomide have been prescribed as steroid-sparing agents.
- Intravenous immunoglobulin is another medication used for pyoderma gangrenosum, with variable clinical efficacy.
- The tumor necrosis factor-alpha inhibitor biologics, such as infliximab, adalimumab, and etanercept, can be used successfully in more difficult cases of pyoderma gangrenosum patients who do not respond to previous therapies. There is a movement to use these medications earlier in the course of the disease to decrease the risks associated with steroids and other immunosuppressants.

Fig. 22.38 A small, evolving ulcer of pyoderma gangrenosum, which can be extremely painful. The indurated border with vascular congestion and surrounding erythema is characteristic and can help distinguish the ulcers of pyoderma gangrenosum from other ulcers.

Fig. 22.39 Pyoderma gangrenosum characterized by a large, painful, ulcer with an asymmetric sharp border and undermined edge. There is yellow, fibrinous debris covering the ulcer and focal areas of granulomatous tissue within.

Fig. 22.40 Pyoderma gangrenosum. The initiating lesion consists of discrete pustules surrounded by an inflammatory areola. The lesion then degenerates into an ulcer.

Fig. 22.41 Pyoderma gangrenosum. Differentiation from other diseases causing ulcers is sometimes very difficult. Malignancies may present as ulcers with exactly the same appearance. Therefore, a biopsy is justified.

Topical Therapy

- Intralesional steroids can be used for small or single lesions, but care must be taken not to injure the skin.
- Local wet dressings (not wet to dry) with Burrow's solution or silver nitrate two or three times daily.
- Superpotent topical steroids and Protopic 0.1% ointment have been used with success.

Fig. 22.42 Pyoderma gangrenosum. The legs are the most common site. New lesions form at sites of injury in a phenomenon called "pathergy." The new lesions become much larger than the lesion created by the initial injury.

Course and Prognosis

- In general, many patients with pyoderma gangrenosum have a chronic relapsing course, even with adequate treatment.
- Although eradication of the disease is the ultimate treatment goal, most regimens are aimed at preventing relapse and flare of the disease as well as reducing or removing steroid therapy.

Fig. 22.43 Pyoderma gangrenosum. Eventually a lesion forms with multiple ulcers with crater-like holes. This is a highly characteristic feature. The lesions consist of small fistula tracks from which pus can be obtained with pressure.

Fig. 22.44 Pyoderma gangrenosum. A huge ulcer is shown with the characteristic violaceous border. Lesions are most often found on the legs but can occur on any skin surface.

Lasers in Dermatology 23

M. Shane Chapman

Introduction

- Laser is an acronym for light amplification by the stimulated emission of radiation.
- Laser light is a monochromatic (single wavelength), coherent (waves in phase), and collimated (waves travel in parallel) form of energy.
- In the skin, laser energy is absorbed by chromophores, which include water, melanin, oxygenated hemoglobin, and certain tattoo pigments.
- Newer, more modern laser technology uses selective photothermolysis to improve outcomes and reduce thermal damage and potential scarring.

Uses of Lasers in Dermatology

Pigmentation

- Lentigos, or solar freckles, usually on sun-exposed areas of the face and hands.

Blood Vessels

- Facial telangiectasias, especially in patients with rosacea of the malar cheeks.
- Hemangiomas can be treated with laser technology, including large and small growths.
- Port wine stains can be treated with the pulsed dye laser.
- Multiple treatments are usually required for complete or nearly complete removal.

Hair Removal

- The alexandrite laser, diode laser, and intense pulsed light can be used to destroy hair follicles.
- Coarse, darkly pigmented hair can be removed with laser light on light-skinned individuals.
- Pseudofolliculitis barbae can be treated with Nd:YAG laser, reducing hair without destroying skin pigment.
- Light, blonde, red, white, and gray hair cannot be removed with laser technology.

Tattoo Removal

- Some types of tattoo ink or pigment, especially the dark pigments, can be removed with laser.
- Multiple treatments are usually required, and the lighter tattoo pigments may not be able to be removed with laser.
- The picosecond laser produces pulses that cause enough pressure on the ink particles that they shatter into smaller particles. This

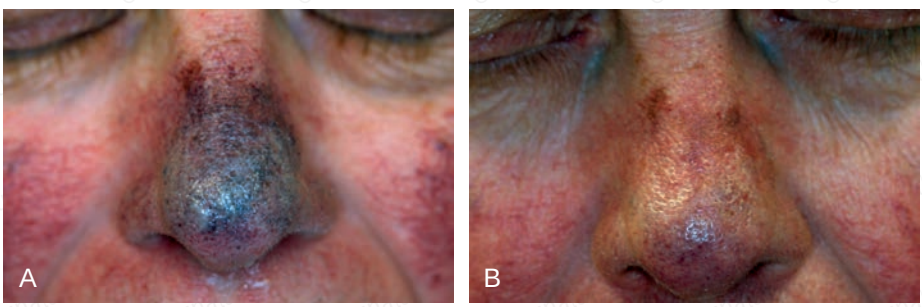

Fig. 23.1 Uses of lasers in dermatology. Dark-red to violaceous telangiectasias over the nose before **(A)** and after **(B)** three treatments with the pulsed dye laser.

laser is capable of removing both darker and lighter colors.

Wrinkles and Rhytids (Skin Tightening)

- The reduction of fine lines, wrinkles, and rhytids and overall skin tightening can be accomplished by several varieties of lasers.
- Carbon dioxide (CO_2) resurfacing, ablative fractionated laser, and erbium YAG lasers are resurfacing lasers that ablate or heat the epidermal layer of skin, causing injury to the dermis that stimulates collagen in the dermis, decreases the visibility of fine lines, and ultimately tightens the skin.
- Resurfacing procedures are ablative in nature; therefore, more risk is involved with these lasers because depigmentation, blistering, and even scarring are possible.

Destruction and Ablation

- Ablative CO_2 lasers use water as the chromophore and can be used to destroy warts, benign tumors, and skin cancers.

Wavelengths

- 308 nm: High-dose targeted laser light, similar to narrow-band ultraviolet light, is used to treat psoriasis and vitiligo.
- 500–1200 nm: Intense pulsed light (IPL) is a light source with a range of 500 to 1200 nm that has multiple uses, including superficial melanin pigment removal, hair removal, and telangiectasia removal.

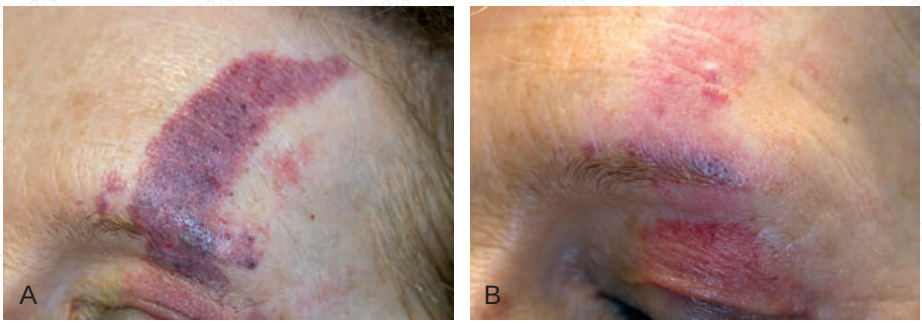

Fig. 23.2 Uses of lasers in dermatology. Long-standing port wine vascular stain on the left forehead before **(A)** and after **(B)** two treatments with the pulsed dye laser.

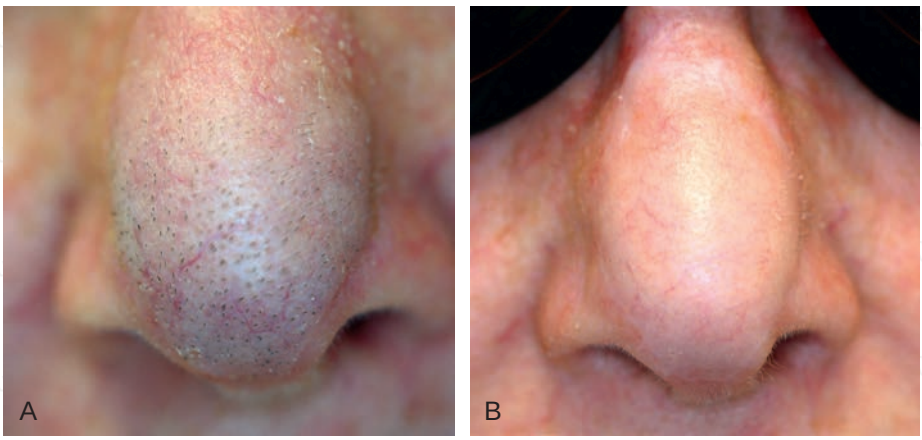

Fig. 23.3 Uses of lasers in dermatology. **A,** This patient had a paramedian forehead flap to cover the nasal tip defect after Mohs' surgery for a basal cell carcinoma. Dark, terminal scalp hair was included in the flap, which was treated with shaving by the patient. **B,** The complete hair removal after five treatments with the alexandrite laser.

- 532 nm: KTP (potassium titanyl phosphate) laser that has double the frequency of the Nd:YAG wavelength and is used to treat various vascular lesions, including port wine stains.
- 585–595 nm: Pulsed dye laser light that is used to treat various types of vascular lesions, including telangiectasias, hemangiomas, and port wine stains.
- 755 nm: Alexandrite laser that is used to remove coarse pigmented hair in light-skinned individuals.
- 1064 nm: Nd:YAG laser is used to treat some spider veins and remove hair in dark-skinned individuals.
- 10,600 nm: Carbon dioxide laser that is used to ablate or resurface the skin for skin tightening, removal of wrinkles, and ablation of warts and other tumors, both benign and malignant.
- Fractionated laser: A laser technology that promotes laser ablation by producing regular lattice of microscopic columns within the skin, allow the laser effect but with a faster recovery than traditional ablative lasers, with less down time and better results than nonablative lasers.

Complications and Limitations

- Burning and scarring with any laser type or technology is possible with excessive energy or fluence.
- Pigment change, both hypopigmentation and hyperpigmentation, can occur after laser surgery.
- Ablation, destruction, or burning of the retinal and iris pigment is possible with several types of lasers.
- Burning or blistering darker skin or tanned skin can occur with several types of lasers.

Table 23.1 Cutaneous Laser Chart

Type of Laser	Wavelength (nm)	Uses
Intense pulsed light	500–1200	Multiple: pigment and hair removal, some vascular lesions, photorejuvenation
KTP (potassium titanyl phosphate)	532	Some vascular lesions, tattoos
Pulsed dye laser	595	Vascular lesions
Alexandrite laser	755	Hair removal in light skin
Nd:YAG (neodymium-doped yttrium aluminum garnet)	1064	Vascular lesions, hair removal in dark skin, tattoos
Carbon dioxide (CO_2) laser	10,600	Cutaneous resurfacing, destruction of skin tissue

24 Leishmaniasis

James G. H. Dinulos

Description

- Leishmaniasis is a parasitic, protozoal infection transmitted by an arthropod bite and acquired in tropical and subtropical areas of the world.

History

- Leishmaniasis is caused by an intracellular infection by protozoa of the genus *Leishmania.*
- The prevalence is estimated at 12 million people worldwide, with an annual incidence of 1.5 million worldwide. Roughly half of all new cases are in children.
- The incidence is increasing as a result of travel, war, and ineffective control of sandfly vectors and mammalian reservoirs.
- Leishmaniasis is considered endemic in tropical and subtropical areas of South America, Asia, Africa, and the Mediterranean basin.
- Leishmaniasis is classified by the geographic area where the infection is acquired, by the specific causative *Leishmania* species, by the arthropod vector, and by the clinical presentation.
- Old World leishmaniasis (acquired in Europe, Asia, and Africa) is caused by *Leishmania* species *L. tropica, L. aethiopica, L. major, L. infantum,* and *L. donovania,* all of which are transmitted by the *Phlebotomus* species of sandfly.
- New World leishmaniasis (acquired in the Americas) is caused by *L. mexicana, L. amazonensis, L. braziliensis, L. guyanensis, L. peruviana, L. panamensis, L. pifanoi, L. garnbami, L. venezuelensis, L. columbiensis,* and *L. chagasi,* all of which are transmitted by the *Lutzomyia* species of sandfly.
- The four clinical presentations of leishmaniasis are cutaneous (skin only), mucocutaneous (skin and mucosal surfaces), diffuse cutaneous, and visceral (involvement of reticuloendothelial organs, also known as *kala azar* or *black fever*).
- The causative protozoan *Leishmania* are found in a flagellated promastigote stage within the midgut of the sandfly vector and transmitted to human hosts at the time of bite by the female sandfly.
- The parasite transforms into an amastigote form within macrophages and multiplies by binary fission and then spreads to other host macrophages.
- Sandfly vectors acquire the parasite by ingesting (blood meal) infected macrophages from an infected host.
- The incubation time from bite to clinical lesion ranges from 1 to 24 months.
- The clinical spectrum of leishmaniasis depends on the cell-mediated immune response of the host to the infection.
- A brisk, effective immune response confines the infection to the skin and leads to resolution of the infection.
- A less effective immune response in a compromised host will allow for disseminated lesions to occur at distant mucosal and visceral sites.

Fig. 24.1 *Phlebotomus* sandfly vector for Old World leishmaniasis. (© World Health Organization, 2010. All rights reserved.)

Fig. 24.2 Raised violaceous plaques of active cutaneous leishmaniasis on the dorsal hand. Note the central ulceration of plaques. (© World Health Organization, 2010. All rights reserved.)

Fig. 24.3 Mucocutaneous leishmaniasis with extensive involvement of the mucosal lips and destruction of nasal cartilage. (© World Health Organization, 2010. All rights reserved).

Skin Findings

Cutaneous Leishmaniasis

- Cutaneous leishmaniasis is the most common form and is characteristic of Old World leishmaniasis.
- The sandfly bite develops into a red 2- to 4-mm, nonpainful papule

Fig. 24.4 Mucocutaneous leishmaniasis with marked local destruction of the nose and upper lip. (© World Health Organization, 2010. All rights reserved).

- Multiple bites produce multiple lesions.
- The prototypical papule slowly enlarges over 2 to 3 months into a 2- to 4-cm plaque with central crusted ulceration and a raised, firm, and violaceous border. The plaque persists for several months.
- Satellite papules are often present. Subcutaneous nodules along regional lymphatics are less common.
- The plaque tends to heal spontaneously with an atrophic scar.

Mucocutaneous Leishmaniasis

- Cutaneous disease extends to involve the nasopharyngeal tissue.
- Mucocutaneous leishmaniasis (New World leishmaniasis) may coexist with cutaneous lesions or arise years after skin lesions have resolved.
- The characteristic painful inflammation and hemorrhage destroy nasal and oral mucosae. This form is called *espundia*.

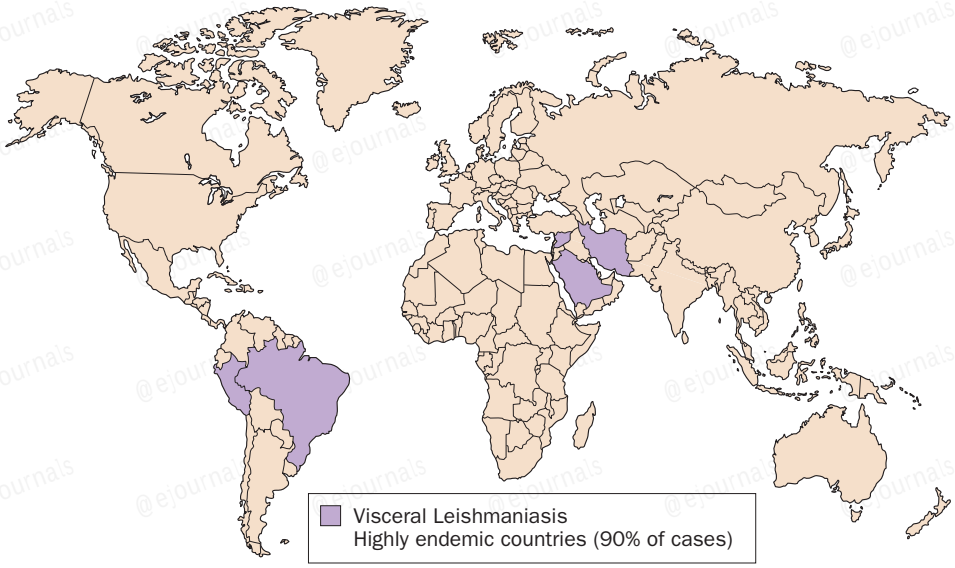

Fig. 24.5 World map showing where cutaneous leishmaniasis is highly endemic in tropical regions. *Lutzomyia* sandflies are the vector in the Americas, whereas *Phlebotomus* sandflies transmit the *Leishmania* parasite in Old World countries. (© World Health Organization, 2010. All rights reserved.)

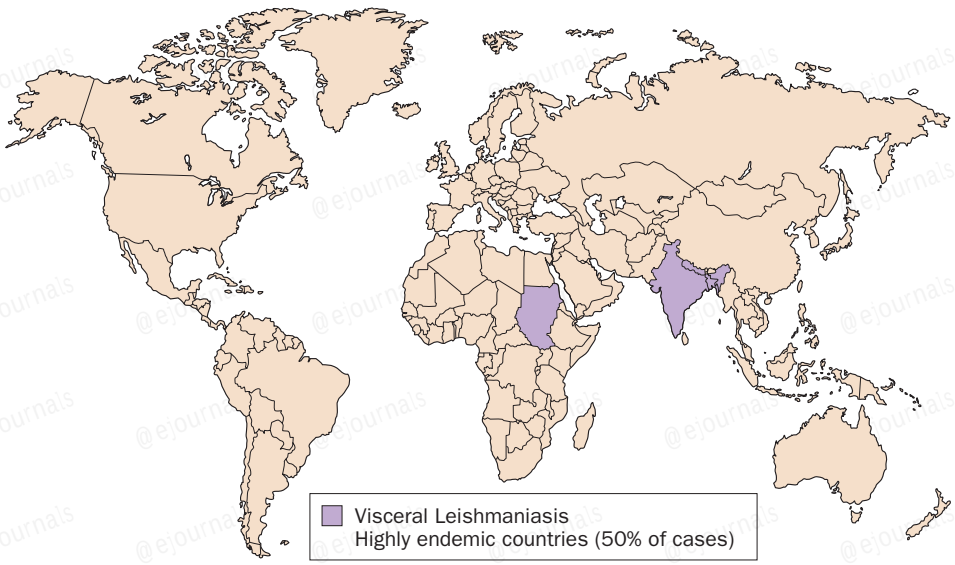

Fig. 24.6 World map identifying regions in Africa and Asia where visceral leishmaniasis is endemic. (© World Health Organization, 2010. All rights reserved.)

Fig. 24.7 A, Cutaneous leishmaniasis of the right lower leg. Note the central dry ulceration with overlying crust and satellite papules. **B,** Diffuse cutaneous leishmaniasis of the left lower leg with multiple granulomatous, centrally ulcerated papules.

Diffuse Cutaneous Leishmaniasis

- Numerous cutaneous parasites produce perilesional satellite papules that develop into nonulcerating nodules (keloid-like).
- Patients with poor cellular immune response to the parasite develop diffuse cutaneous leishmaniasis.

Nonskin Findings

Visceral Leishmaniasis (Kala Azar)

- Kala azar involves bone marrow, liver, and spleen.
- The incubation period is 1 to 36 months. Progression may be fast or gradual.
- Patients develop fever, pain, lymphadenopathy, and hepatosplenomegaly.
- Pancytopenia may occur.

Laboratory

- Giemsa's, Brown-Hopps, Gram's, or Leishman's stains enhance *Leishmania* organisms on touch preparations. This is a rapid and practical test.
- Skin biopsy from the edge of a lesion or ulcer shows 2- to 4-micron amastigotes within dermal macrophages. Giemsa's stain enhances the organisms.
- Polymerase chain reaction (PCR) is a highly sensitive and rapid test.
- Culture of infected skin in Novy-MacNeal-Nicolle medium will produce promastigote forms in 21 days. The species of the parasite can be identified.
- Detection of serum antibodies to the recombinant K39 antigen of leishmaniasis is a sensitive (95%–100%) method for the diagnosis of active, visceral leishmaniasis.

Course and Prognosis

- Localized disease has a better prognosis than diffuse disease.
- Patients with compromised cellular immunity have a poorer prognosis.

Fig. 24.8 A, B, New lesions of cutaneous leishmaniasis showing a raised granulomatous, undermined border and central ulceration. Skin biopsy of the lesion border with Giemsa's stain will confirm parasites within dermal macrophages.

Differential Diagnosis

- Pyoderma gangrenosum
- Squamous cell carcinoma
- Leprosy
- Psoriasis
- *Mycobacterium marinum* infection

Treatment

- *Leishmania major* (e.g., Iraq) is self-limited and heals within 12 months with minimal scarring. Treatment in most cases is not necessary.
- *Leishmania tropica* (e.g., Afghanistan) may cause aggressive or chronic disease, requiring treatment.

- Local treatment options include cryotherapy (liquid nitrogen), thermotherapy (local heat therapy at 40° to 42°C with, e.g., a device called ThermoMed), topical paromomycin (various preparations), and intralesional meglumine antimoniate or sodium stibogluconate.
- Systemic therapy options include pentavalent antimonials (e.g., meglumine antimoniate, sodium stibogluconate). Pentavalent antimonials are drugs of choice.
- Other systemic therapies include liposomal amphotericin B, azole antifungals, dapsone, rifampin, and allopurinol.
- Access to and proper monitoring for toxicity from some of these agents may require the assistance of an infectious disease specialist and the Centers for Disease Control and Prevention.

Pearl

- Referral to a qualified infectious disease specialist should be considered, especially for patients with a compromised immune system or suspected visceral involvement.

Fig. 24.9 Leishmaniasis causes pseudoepitheliomatous hyperplasia and can mimic squamous cell carcinoma. Patients should provide a thorough travel history.

25 Leprosy (Hansen's Disease)

M. Shane Chapman

Description

- Leprosy, or Hansen's disease, is a chronic infection caused by the bacteria *Mycobacterium leprae*.
- The disease infects the skin and nervous system primarily, leading to visible skin lesions and autoamputation of the fingers and toes, and thus to disability and social stigmatization.
- It is a common infectious disease in Asia, Africa, and Central and South America, affecting millions of people.

History

- Leprosy has been recorded in historical documents since 600 BC.
- Genomic comparison studies suggest that the infection may have originated in East Africa.
- The cultures of ancient Egypt, China, India, and Japan all have documentation of the disease.
- Biblical mentions of psoriasis, vitiligo, and eczema may have actually been descriptions of leprosy.
- It is postulated that Alexander the Great brought the disease from India to the Greek and Roman Empires.
- Leprosy was endemic in Europe during the Middle Ages.
- Exploration in the 15th and 16th centuries led to its spread to the Americas.

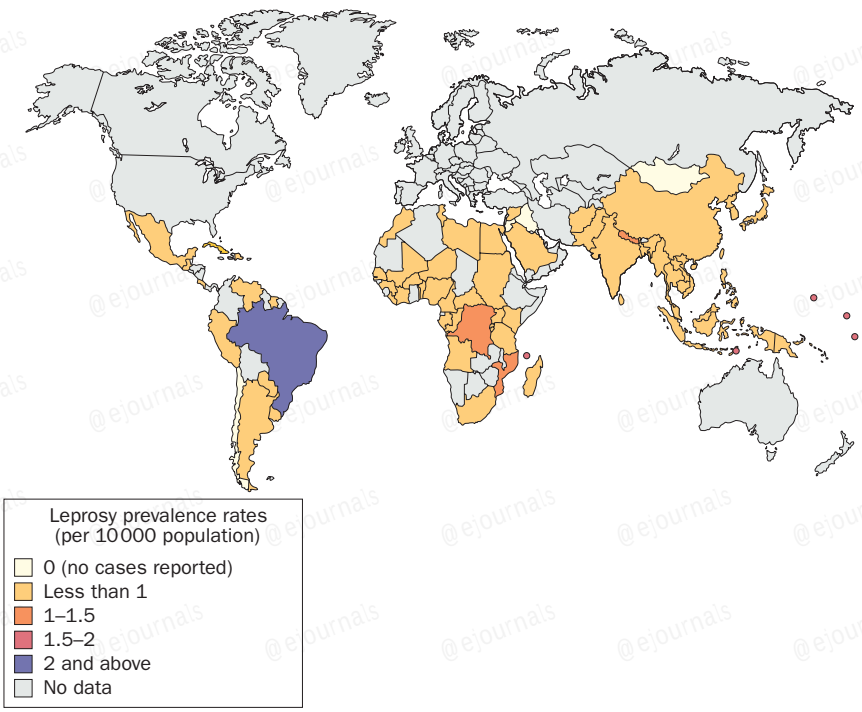

Fig. 25.1 The geographic distribution of leprosy cases across the world. Brazil, sub-Saharan Africa, and parts of Asia have the most cases per population. (From www.who.int; © World Health Organization, 2012. All rights reserved.)

Fig. 25.2 Leprosy. This young woman has a swollen preauricular nodule or peripheral nerve that is easily palpable and visible, a common characteristic of leprosy. (© World Health Organization, 2010. All rights reserved.)

Fig. 25.3 Leprosy. Facial papules and nodules cover the face of this patient. This degree of papules and nodules is typically seen in the more advanced forms of the infection or lepromatous form. The granulomatous infiltrate may involve the mucosa as well as the skin. There is also noticeable hair loss, especially of the lateral eyebrows, also typical of leprosy. (© World Health Organization, 2010. All rights reserved.)

- Danielssen and Boeck have been credited with the first Western description of leprosy.
- Gerhard Henrik Armauer Hansen collected extensive clinical, epidemiologic, and microbiologic studies of the *M. leprae* organism and is the namesake associated with the modern name of the disease (1870s).
- Mitsuda devised the first skin test for leprosy (1919).
- Faget recorded the positive effects of sulfonamides in the treatment of disease.
- Rabello described the notion of polar forms of leprosy (1938).
- Ridley and Jopling created a classification system also based on polar forms (1966).
- The World Health Organization (WHO) classification divides leprosy into paucibacillary and multibacillary disease (1997).

Skin Findings

- There is a spectrum of skin findings in patients with leprosy, depending on the

Fig. 25.4 Leprosy. This patient has slightly elevated and hypopigmented patches on his back. He most likely has multibacillary leprosy or the borderline variant of the disease. (© World Health Organization, 2010. All rights reserved.)

Fig. 25.5 Leprosy. Flat, anesthetic hypopigmented patches are scattered across the trunk of this young boy; these are more common in the paucibacillary or tuberculoid forms of leprosy. (© World Health Organization, 2010. All rights reserved.)

stage and host immune system: lepromatous, borderline-lepromatous, borderline-borderline, borderline-tuberculoid, and tuberculoid.

Lepromatous Leprosy

- The lepromatous leprosy form of the disease tends to be the most inflammatory and dramatic because it is related to the greatest number of bacilli (multibacillary) and the least effective cellular immune response.
- Lepromatous leprosy shows inflamed macules, papules, nodules, and plaques, symmetrically distributed over the face, ears, wrists, elbows, knees, and buttocks.
- The mycobacterium prefers cooler areas, so areas such as the ears, elbows, and knees can contain large numbers of mycobacteria when a skin slit is performed.
- These lesions may be anesthetic and hypopigmented.
- Leonine facies occurs with extensive infiltration of the forehead and lower face.
- Saddle nose deformity, madarosis, epistaxis, enlarged earlobes, scarring of the testes, gynecomastia, and ichthyosis can also occur in this form of leprosy.
- This clinical form also correlates with multibacillary disease.

Borderline Leprosy

- Borderline leprosy tends to be the most common form of the disease.
- Lesions in this form of leprosy vary on the polarity of the immune response, either toward the lepromatous or the tuberculoid form.
- Skin lesions are similar to the tuberculoid variant but are more numerous and larger and tend to affect the peripheral nervous system.
- This variant of leprosy is considered unstable and can move toward the tuberculoid variant or revert to the more severe lepromatous variant.

Tuberculoid Leprosy

- Tuberculoid leprosy patients typically have a few patches or plaques that are less elevated, are anesthetic or hypesthetic, and can be either hypopigmented or hyperpigmented.
- These patches usually occur on the trunk and extremities.
- Pain, muscle weakness of the hands and feet, dry skin, and enlarged nerves, especially the ulnar and peroneal nerves, are common.
- Loss of the fingers and toes is common.
- Blindness can also occur.
- This variant of leprosy is considered to be paucibacillary.

Nonskin Findings

- Enlarged palpable peripheral nerves: greater auricular, ulnar, radial, common peroneal, and posterior tibial nerves are characteristic and aid in making clinical diagnosis.
- Decreased sensation to pain, temperature, and touch is common.
- Muscle atrophy, contractures of the fingers (especially the 4th and 5th digits).
- Dry eyes and dry nose mucosa.

Laboratory and Testing

- A skin biopsy shows a characteristic granulomatous infiltrate and involvement of the peripheral nerves.
- Special staining with the acid-fast stain may show the bacilli, but this is sometimes difficult and not reliable.
- Skin slits can be made on the earlobes, elbows, and knees, and blood from the patient placed on a glass slide and stained appropriately can show the bacilli, but this is also not reliable in some patients with the tuberculoid form of the disease.
- *M. leprae* is unable to be cultured in hospital laboratories. The bacilli can be injected into other animals and cultured in this manner. The mouse footpad is a common method of culture for studying the disease.

Course and Prognosis

- The course of untreated leprosy can take the form of tuberculoid to borderline to lepromatous, and revert back and forth, depending on the host's immune response to the bacilli.
- The skin becomes infected and shows anesthetic patches, plaques, and nodules. Nerves of the digits become infected and lead to anesthetic fingers and toes. These digits can become injured and traumatized without the patient recognizing the pain, ultimately causing scarring and destruction of the soft tissues and bones of the digits.
- Blindness, alopecia, destruction of the oral and nasal cavity, testicular atrophy, and immobility are other common manifestations of untreated leprosy.
- If treated with the multidrug therapy (MDT) regimen of dapsone, rifampicin, and clofazimine, patients can prevent this course of infection.
- Leprosy reactions are the main cause of acute nerve damage and disability in leprosy. Reactions are caused by changes in the immune response. There are two types of reaction: reversal reaction, or type 1; and erythema nodosum leprosum (ENL), or type 2.
- Reversal reactions often occur in the first 6 months of MDT and may occur in both paucibacillary and multibacillary leprosy but are more common in MB.
- Some patients are found to have reversal reactions at the time of diagnosis, and it may be the symptoms of the reaction that make the patient aware of the disease. A reversal reaction may occur after completion of MDT, particularly when short-duration regimens are used.

Differential Diagnosis

- The hypopigmented patches of leprosy can mimic vitiligo
- Leonine facies can resemble an advanced infiltrative form of cutaneous T-cell lymphoma
- Throughout history, patients with tinea, psoriasis, and eczema were often misdiagnosed as having leprosy

Treatment

- Until the development of dapsone in the 1940s, there was no effective treatment of leprosy.
- Dapsone, as monotherapy, is a weak bactericidal drug; patients were required to take the drug indefinitely, and resistance developed.
- Clofazimine and rifampicin were introduced in the 1960s and used in combination with dapsone.
- MDT with these three medications is still used today.
- A 12-month regimen using all three drugs for multibacillary disease, and a 6-month course of dapsone and rifampin for paucibacillary disease, is standard.
- In severe reversal reactions, prednisone and thalidomide can be used to treat the inflammatory immune response.
- For some patients with a single lesion of leprosy, it is adequate for them to be treated with a single dose of rifampicin, minocycline, or ofloxacin.

Discussion

- Leprosy continues to infect millions of people, mostly the poor, living in crowded conditions of developing countries.

- It continues to carry the most negative medical stigma the world has known.
- In the past, thousands or perhaps millions of patients with leprosy were banished or forcibly confined to remote areas to live away from society, never to return. Today, even though there is curative treatment for the disease, some of those leprosaria still exist because the inhabitants are unable to live in society, owing to disability, stigma, and inability to reconvert back to society.
- Research suggests that patients who acquire leprosy have a defect in cell-mediated immunity that causes an increased susceptibility to the disease. Only 5% to 10% of the world's population is susceptible to infection with disease.

Fig. 25.6 Leprosy. Hypopigmented macules and patches, with slight scale, are scattered diffusely over the trunk of this patient with tuberculoid leprosy. These macules and patches are characteristically anesthetic. (© World Health Organization, 2010. All rights reserved.)

Fig. 25.7 Leprosy. The pink to flesh-colored patch of tuberculoid leprosy resembles eczema or psoriasis, which may delay diagnosis.

Quick Reference Formulary A

(Topical steroids are listed on the inside back cover.)

Acne Medications—Retinoids

Drug Name	Form	Strength/Active Ingredients	Packaging
Tretinoin (generic)	Cream Gel	0.025%, 0.05%, 0.1% 0.01%, 0.025%	20 g, 45 g tube 15 g, 45 g tube
Retin-A Micro	Gel Gel	0.1%/0.04% tretinoin 0.04% tretinoin	20 g, 45 g tube 50 g pump
Tazorac	Gel Cream	0.1%, 0.05% tazarotene 0.1%, 0.5% tazarotene	30 g, 100 g tube 30 g, 60 g tube
Fabior	Foam	0.1% tazarotene	50 g, 100 g can
Adapalene (generic)	Cream Gel Lotion	0.1%, 0.3% 0.1% 0.1%	45 g tube 45 g tube (OTC: Differin) 45 g tube
Epiduo	Gel	0.1% adapalene/2.5% benzoyl peroxide	45 g tube
Epiduo Forte	Gel	0.3% adapalene/2.5% benzoyl peroxide	15 g, 30 g, 45 g, 60 g, 70 g tube
Veltin	Gel	1.2% clindamycin phosphate/0.025% tretinoin	30 g, 60 g tube

Acne Medications—Topical Antibiotics

Drug Name	Strength/Form	Packaging Size
Aczone	7.5% dapsone gel	30 g, 60 g, 90 g pump
Benzaclin	1% clindamycin/5% benzoyl peroxide gel	25 g, 50 g tube 35 g, 50 g pump
Benzamycin	3% erythromycin/5% benzoyl peroxide gel	23.3 g, 46.6 g jar
Clindamycin (generic)	1% gel 1% lotion 1% solution 1% foam 2% cream	30 g, 60 g tube 60 mL bottle 30 mL, 60 mL bottle 50 g, 100 g can 40 g tube
Duac	1.2% clindamycin/5% benzoyl peroxide gel	45 g tube
Sulfacetamide/ sulfur (generic)	10%/5% cleanser 10%/5% lotion 10%/5% foam	6 oz, 8 oz, 12 oz bottle/pump 25 g, 30 g, 60 g tube 60 g can
sodium sulfacetamide (generic)	10% cleanser 10% ointment 10% gel 10% lotion	180 mL, 355 mL, 480 mL bottle 3.5 g tube 355 mL bottle 118 mL bottle

Acne Medications—Benzoyl Peroxide Cleansers*

Product	Formulation	Packaging
Brevoxyl Creamy Wash	Liquid 4%	6 oz tube
Brevoxyl Creamy Wash	Liquid 8%	6 oz tube
PanOxyl 5 bar (OTC)	Bar 5%	4 oz bar
PanOxyl 10 bar (OTC)	Bar 10%	4 oz bar

*Numerous generics, many different concentrations.

Acne Medications: Oral Antibiotics

Generic Drug Name	Preparation	Adult Dosage (mg Unless Noted)
Doxycycline	50/75/100/150 mg	1–2 times per day
Minocycline	50/75/100 mg	1–2 times per day
Minocycline extended-release tablets	55/65/80/105/115 mg	1 tablet every day (1 mg/kg/day)

Topical Treatments for Actinic Keratoses

Brand Name/Form	Strength/Active Ingredients	Packaging
Aldara cream	5% imiquimod	Box of 6, 12, or 24 packets
Efudex solution	2% fluorouracil 5% fluorouracil	10 mL bottle 10 mL bottle
Efudex cream	5% fluorouracil	40 g tube
Picato gel	0.015% ingenol 0.05% ingenol	3 tubes/carton (face) 2 tubes/carton (body)
Zyclara cream	2.5% imiquimod 3.75% imiquimod	7.5 g pump 7.5 g pump/box of 28 packets

Antipruritic Creams and Lotions: Available OTC

Brand Name	Active Ingredient	Packaging
Eucerin itch relief	Menthol 0.15%	6.8 oz spray
Neutrogena anti-itch moisturizer	Camphor 0.1%, dimethacone 0.1%	10.1 oz
Pramoxine	1% pramoxine cream/gel/lotion/spray	4 oz
Sarna original	0.5% each of camphor, menthol	7.5 oz bottle
Sarna sensitive anti-itch lotion	Pramoxine HCl	7.5 oz
Sarna Ultra anti-itch cream	Menthol 0.5% and pramoxine	2 oz
Zonalon	5% doxepin	45 g

Skin Bleaches and Depigmenting Agents

Drug Name	Active Ingredient	Packaging
Hydroquinone	4% hydroquinone	1 oz, 2 oz jar
Tri-Luma	0.01% fluocinolone acetonide/0.05% tretinoin/4% hydroquinone	30 g tube of cream

Genital Warts

Brand Name/Form	Drug Strength	Packaging
Veregen ointment	15% sinecatechins	15 g tube
Condylox solution	0.5% podofilox	3.5 mL bottle
Condylox gel	0.5% podofilox	3.5 g tube
Aldara cream	5% imiquimod	Box of 12 or 24 packets
Zyclara cream	3.75% imiquimod	Box of 28 packets

Psoriasis—Topical Vitamin D_3 Analogs

Brand Name/Form	Drug Strength	Packaging
Dovonex cream	0.005% calcipotriene	60 g/120 g tube
Sorilux foam	0.005% calcipotriene	60 g/120 g can
Vectical ointment	0.0003% calcitriol	100 g tube
Taclonex ointment	0.005% calcipotriene + 0.064% betamethasone	60 g/100 g tube
Taclonex suspension	0.005% calcipotriene + 0.064% betamethasone	60 g/100 g bottle
Enstilar foam	0.005% calcipotriene + 0.064% betamethasone	60 g/120 g can

Antirosacea Medications

Drug	Strength/Form	Packaging
Sodium sulfacetamide/sulfur (generic)	10%/5% cleanser 10%/5% foam 10%/5% cream 10%/5% gel 10%/5% lotion	6 oz, 8 oz, 12 oz bottle 60 g can 28 g, 57 g tube 45 g tube 25 g, 30 g, 60 g tube
Azelex	20% azelaic acid cream	30 g, 50 g tube
Finacea	15% azelaic acid gel 15% azelaic acid foam	50 g tube 50 g can
Klaron	10% sodium sulfacetamide lotion	118 mL bottle
Metronidazole (generic)	0.75% cream 0.75% lotion	45 g tube 59 mL bottle
Metrogel	1% metronidazole gel	60 g tube, 55 g gel pump
Noritate	1% metronidazole cream	60 g tube
Soolantra	1% ivermectin	30 g cream
Mirvaso	0.33% brimonidine tartrate	30 g gel
Rhofade	1% oxymetazoline hydrochloride	30 g cream

Empirical Oral Antibiotic Regimens for Selected Patients with Methicillin-Resistant *Staphylococcus aureus* (MRSA) Infections

Antibiotic	Dose (Adults)
Trimethoprim-sulfamethoxazole	One or two double-strength doses (160 mg of trimethoprim and 800 mg of sulfamethoxazole) twice per day
Clindamycin	300–450 mg three times per day
Doxycycline	100 mg twice per day
Minocycline	200 mg initially, followed by 100 mg every 12 hours

Anti-infectives, Topical

Generic	Strength and Form	Packaging
Bacitracin zinc/polymyxin B (Polysporin)	OTC ointment	3.5 g tube
Neomycin sulfate/polymyxin B sulfate/bacitracin zinc (Neosporin)	OTC ointment	3.5 g tube
Azelaic acid	20% cream	30 g, 50 g tube
Bacitracin	500 units/g ointment	3.5 g of 500 units/g 1 g of 500 units/g
Clindamycin phosphate	1% gel, lotion 1% solution	30 g, 60 g tube 60 mL bottle
Erythromycin	2% gel 2% solution 0.5% ointment	30 g, 60 g tube 60 mL bottle 1 g, 3.5 g tube
Gentamicin	0.1% ointment, cream 0.3% ointment	15 g, 30 g tube 3.5 g tube
Metronidazole	0.75% gel, cream 0.75% lotion 1% gel	45 g tube 59 mL bottle 60 g tube
Mupirocin (Bactroban)	2% cream 2% ointment	15 g, 30 g tube 22 g tube
Retapamulin (Altabax)	1% ointment	15 g, 30 g tube

Isotretinoin (Branded Generics) Accutane—First Brand Name Medicine

Dosage/Form	Generics
10 mg capsule	Absorica, Amnesteem, Claravis, Myorisan, Zenatane
20 mg capsule	Absorica, Amnesteem, Claravis, Myorisan, Zenatane
25 mg capsule	Absorica
30 mg capsule	Absorica, Claravis
35 mg capsule	Absorica
40 mg capsule	Absorica, Amnesteem, Claravis, Myorisan, Zenatane

Dosing Isotretinoin by Body Weight

Body weight		Total mg/day	
Kilograms	Pounds	0.5 mg/kg	1 mg/kg
40	88	20	40
50	110	25	50
60	132	30	60
70	154	35	70
80	176	40	80
90	198	45	90
100	220	50	100

Antiwrinkle Cream

Product	Active Ingredient	Packaging
Renova 0.02% emollient	Tretinoin	40 g
Retin-A	Tretinoin	Many doses: see Acne Medications
Avage 0.1 cream	Tazarotene	30 g

Antifungal Agents, Topical

Drug (Generic)	Strength/Form	Packaging
Butenafine hydrochloride	1% cream	15 g, 30 g tube
Ciclopirox	0.77% cream, lotion, suspension	30 g, 45 g, 100 g tube; 30 mL, 60 mL bottle
Clotrimazole	1% cream, ointment, solution	15 g, 30 g, 45 g tube
Econazole nitrate	1% cream	15 g, 35 g, 85 g tube
Efinaconazole solution (Jublia) for toenails	10% solution	40 mL, 80 mL bottle
Ketoconazole	2% cream, foam	15 g, 30 g, 60 g tube; 50 g, 100 g can
Miconazole nitrate (OTC)	2% cream	1 oz tube
Naftifine hydrochloride	1% cream 2% cream	15 g, 30 g, 60 g, 90 g tube 30 g, 45 g, 60 g tube
Nystatin	100,000 unit/g cream, ointment, powder	15 g, 30 g tube; 15 g, 30 g, 60 g bottle
Oxiconazole nitrate	1% cream	30 g, 60 g, 90 g tube
Sulconazole nitrate	1% cream, solution	15 g, 30 g, 60 g tube; 3 mL bottle
Terbinafine (Lamasil)	1% cream	1 oz tube
Tolnaftate	1% cream, powder, aerosol spray	Various sizes OTC

Antifungal Agents (Oral)

Brand Name	Generic Name	Packaging
Diflucan	Fluconazole	50, 100, 150, 200 mg
Grifulvin V	Griseofulvin microsize	500 mg; 125 mg/5 mL in 4 oz bottle
Gris-PEG	Griseofulvin ultramicrosize	125, 250 mg
Mycostatin	Nystatin	500,000, 1 million unit capsules 100,000 units/mL suspension
Nizoral	Ketoconazole	200 mg
Lamisil	Terbinafine	250 mg
Sporanox	Itraconazole	100 mg
Mycelex troches for oral *Candida*		10 mg troche; bottle of 70 or 140; dissolve 5/day in mouth for 14 days

Antihistamines—H_1-Receptor Antagonists

Drug	Initial Dose (Adult)	Maximal Dose (Adult)	Liquid Formulation	Tablet Formulation
Nonsedating				
Fexofenadine (Allegra)	180 mg daily	180 mg twice a day	—	30, 60, 180 mg
Desloratadine (Clarinex)	5 mg	10 mg	—	5 mg
Loratadine (Claritin)	10 mg daily	20 mg twice a day	5 mg/5 mL	10 mg
Cetirizine (Zyrtec)	10 mg daily	10 mg twice a day	5 mg/5 mL, 1 mg/mL	5, 10 mg
Sedating				
Hydroxyzine (Atarax)	10 mg four times a day	50 mg four times a day	10 mg/5 mL suspension, 25 mg/5 mL	10, 25, 50, 100 mg
Diphenhydramine (Benadryl)	25 mg twice a day	50 mg four times a day	Elixir 12.5 mg/5 mL; syrup 6.25 mg/5 mL	25, 50 mg; 12.5 mg chewable tablet
Cyproheptadine (Periactin)	4 mg four times a day	8 mg four times a day	2 mg/5 mL	4 mg

Antiperspirants

Brand Name	Active Ingredient	Packaging
CertainDri (OTC)	Aluminum chloride (hexahydrate)	1, 2 oz roll-on, pump spray (nonaerosol)
Drysol (Rx)	20% aluminum chloride (hexahydrate) in 93% anhydrous ethyl alcohol	35 mL bottle with Dab-O-Matic applicator; 37.5 mL bottle
Hypercare	20% aluminum chloride (hexahydrate) in 93% anhydrous ethyl alcohol	37.5 mL bottle; 35 and 60 mL bottles with Dab-O-Matic applicator
Lazerformalyde solution (Rx)	10% formaldehyde	3 oz roll-on
Formaldehyde-10 spray	10% formaldehyde	2 oz spray bottle
Xerac AC (Rx)	6.25% aluminum chloride (hexahydrate) in 96% anhydrous ethyl alcohol	35, 60 mL bottles with Dab-O-Matic applicator

Antiviral Agents (Herpes Simplex and Zoster)

Brand (Generic)	Dosage Form
Abreva (docosanol)	2 g tablet (OTC)
Denavir (penciclovir)	1.5 g ointment
Famvir (famciclovir)	125, 250, 500 mg tablets
Valtrex (valacyclovir)	500 mg, 1 g capsules
Zovirax (acyclovir)	200, 400, 800 mg capsules 200 mg/5 mL suspension

Masking Agents (Cosmetic Covering Agents)

Brand Name	Base	Packaging	Shades
Covermark*	Cream	Many products	9–10
Dermablend cover cream*	Cream	Many products	21

*Waterproof concealing makeup.

Hair Restoration Products

Brand Name	Active Ingredient	Dosage Form
Propecia	Finasteride	1 mg tablet
Generic	Finasteride	5 mg (split 5 mg tablet into 4 parts); a great cost saving
Avodart	Dutasteride	0.5 mg (not FDA approved)
Rogaine	Minoxidil solution	Solutions and foam, 2% for women and men, 5% for men

Immunomodulators (Topical)

Steroid-Free Topical Anti-inflammatory Agents

Drug Name	Active Ingredient	Packaging
Elidel cream	Pimecrolimus 1%	15 g, 30 g, 100 g tube
Protopic ointment 0.1%	Tacrolimus 0.1%	30 g, 60 g, 100 g tube
Protopic ointment 0.3%	Tacrolimus 0.3%	30 g, 60 g, 100 g tube

Antiseborrheic Preparations

Brand Name	Active Ingredient	Packaging
Loprox gel	Ciclopirox	45 g tube
Nizoral cream	Ketoconazole	15, 30, 60 g tube
Ovace wash	10% sulfacetamide sodium	6 oz/12 oz bottle
Ovace foam	10% sulfacetamide sodium	50 g/100 g can
Carmol scalp treatment lotion	10% sulfacetamide sodium	90 g bottle
Promiseb cream	Castor oil, disodium EDTA, PEG-30	30 g tube

Corticosteroid and Tar Scalp Preparations

Brand Name	Active Ingredient	Base	Packaging
Derma-Smoothe/FS (Rx)	Fluocinolone acetonide 0.01%	Peanut oil	120 mL
10% liquor carbonis detergens in Nivea oil*	Liquor carbonis detergens; 8, 16 oz	Nivea oil	Prescribe

*Pharmacist compounded.

Tar-Containing Bath Oil (or Applied Directly to Lesions)

Brand Name	Strength	Packaging
Balnetar	2.5% coal tar	240 mL
Cutar emulsion	7.5% LCD	6 oz, 1 gal
Doak Oil	2% tar distillate	240 mL
Doak Oil Forte	5% tar distillate	120 mL
Polytar Bath	25% polytar	240 mL
Zetar emulsion (Rx)	30% whole coal tar	177 mL (6 oz)

Scabicides

Brand Name	Generic/Strength/Form	Packaging
Elimite	Permethrin 5% cream	60 g tube
Kwell	Lindane 1% lotion	16 oz bottle
Kwell	Lindane 1% shampoo	60 mL bottle
Sulfur	Sulfur 5%–10% ointment	Various quantities
Stromectol	Ivermectin 3 mg	3 mg tablets

Pediculocides

Brand	Generic Name	Packaging
NIX cream rinse	Permethrin	2 oz
Ovide	0.5% malathion	2 oz lotion
RID (OTC)	0.3% pyrethrins	2 oz, 4 oz; 1 gallon liquid
Sklice	0.5% ivermectin	117 g tube
Spinosad	0.9% spinosad	120 mL

Biologic and Related Medications—FDA Approved for Treatment of Psoriasis

Generic (Brand)	Mechanism	Route	Dose and Administration
Infliximab (**Remicade**)	TNF-alpha blocker	IV	100 mg VIAL to be drawn at infusion center *Induction:* 5 mg/kg on weeks 0, 2, and 6 *Maintenance:* 5 mg/kg every 8 weeks
Etanercept (**Enbrel**)	TNF-alpha blocker	SC	50 mg PEN or Prefilled SYRINGE *Induction:* Inject 50 mg twice weekly for 3 months *Maintenance:* Inject 50 mg ***once*** weekly **OR** 50 mg ***twice*** weekly For pediatric patients 4–17 years old with chronic moderate to severe plaque psoriasis. No induction dose needed. Weekly dosing by weight: <138 lb (63 kg) = 0.8 mg/kg ≥138 lb (63 kg) = 50 mg Injection options by weight: <68 lb = 25 mg VIAL 68 lb to <138 lb = 25 mg VIAL or Prefilled SYRINGE ≥138 lb = 25 mg VIAL, 25 mg or 50 mg Prefilled SYRINGE, or SureClick Autoinjector
Adalinumab (**Humira**)	TNF-alpha blocker	SC	40 mg PEN or Prefilled SYRINGE *Induction:* Inject 80 mg day 1, 40 mg day 8, and 40 mg day 22 *Maintenance:* Inject 40 mg every other week
Ustekinumab (**Stelara**)	Interleukin 12/23 inhibitor	SC	45 mg (≤220 lb) **OR** 90 mg (>220 lb) Prefilled SYRINGE to be administered in office *Induction:* Inject 1 pen on day 0 and day 28 *Maintenance:* Inject 1 pen every 12 weeks
Secukinumab (**Cosentyx**)	Interleukin 17-A inhibitor	SC	150 mg PEN or Prefilled SYRINGE *Induction:* Inject 300 mg week 0, 1, 2, 3 *Maintenance:* Inject 300 mg every 4 weeks
Ixekizumab (**Taltz**)	Interleukin 17-A inhibitor	SC	80 mg PEN or Prefilled SYRINGE *Induction:* Inject 160 mg week 0, then 80 mg weeks 2, 4, 6, 8, 10, 12 *Maintenance:* Inject 80 mg every 4 weeks
Apremilast (**Otezla**)	Phosphodiesterase 4 inhibitor	PO	*Titration:* (comes in prefilled pack) Day 1: 10 mg in morning Day 2: 10 mg in morning and 10 mg in evening Day 3: 10 mg in morning and 20 mg in evening Day 4: 20 mg in morning and 20 mg in evening Day 5: 20 mg in morning and 30 mg in evening Day 6 and thereafter: 30 mg twice daily *Maintenance:* 30 mg twice a day
Broadlumab (**SILIQ**)	Interleukin 17-A inhibitor	SC	210 mg Prefilled SYRINGE *Induction:* Inject 210 mg week 0, 1, and 2 *Maintenance:* Inject 210 mg every other week

Biologic and Related Medications—FDA Approved for Treatment of Psoriasis—cont'd

Generic (Brand)	Mechanism	Route	Dose and Administration
Guselkumab (**Tremfya**)	Interleukin 23 blocker	SC	100 mg Prefilled SYRINGE *Induction:* Inject 100 mg week 0, 4, and every 8 weeks thereafter *Maintenance:* Inject 100 mg every 8 weeks

Tests to Consider Before Initiating and During Biologic Therapy

TB—skin or *Mycobacterium tuberculosis* tuberculin stimulated gamma interferon [Presence] in blood
Basic metabolic 2000 panel—serum or plasma
CBC with autodifferential panel—blood
Hepatic function 2000 panel—serum or plasma
Hepatitis B and C; and HIV

New Medications FDA Approved for Treatment of Atopic Dermatitis

Generic (Brand)	Mechanism	Route	Dose and Administration
Dupilumab (**Dupixent**)	Interleukin 4 and 13 inhibitor	SC	300 mg Prefilled SYRINGE *Induction:* Inject 600 mg on day 1 *Maintenance:* Inject 300 mg every other week
Crisaborole (**Eucrisa**)	Phosphodiesterase-4 inhibitor	Topical	60 g, 100 g tube, 2% ointment Apply a thin layer to affected areas BID

Formulary updated by Shyla M. Stone, CMA, M.ED.

Dietary Recommendations

For the prevention and improvement of:

ACNE
DEPRESSION
VASCULAR DISEASE
DEMENTIA AND ALZHEIMER'S DISEASE

Do Eat...

- Six or more servings of leafy green vegetables every week. (Almost a salad a day.)
- At least one serving of another vegetable every day.
- More than two servings of berries every week.
- More than five servings of nuts every week. (Try them as a daily snack.)
- Extravirgin olive oil instead of butter and as your primary cooking oil.
- More than three servings of whole grains every day.
- Fish that hasn't been fried for at least one meal every week.
- Beans for more than three meals every week. (That is, eat beans roughly every other day.)
- Poultry for more than two meals every week.

Do Limit...

- Butter to one tablespoon every day.
- Cheese to less than one serving every week.
- Red meat to fewer than four meals every week.
- Fried foods and fast food to less than one serving every week.
- Sweets and pastries to fewer than five servings every week.
- **FOR ACNE**: Also limit intake of milk and milk products especially skim milk.

Corticosteroids (Topical)

Group*	Brand Name or Generic Name†	Drug Strength (%)	Generic Name	Drug Sizes‡
I	Clobex spray	0.05	Clobetasol propionate	59, 125 mL
	Clobex lotion	0.05	Clobetasol propionate	59, 118 mL
	Cordran tape	4 mcg/SQCM	Flurandrenolide	3×24, 3×80 roll
	Cormax cream	**0.05**	**Clobetasol propionate**	**15, 30, 45 g**
	Cormax ointment	**0.05**	**Clobetasol propionate**	**15, 30, 45 g**
	Cormax scalp solution	**0.05**	**Clobetasol propionate**	**515, 500 mL**
	Ultravate cream	**0.05**	**Halobetasol propionate**	**15, 50 g**
	Ultravate ointment	**0.05**	**Halobetasol propionate**	**15, 50 g**
	Ointment	**0.05**	**Augmented betamethasone dipropionate**	**15, 45 g**
	Cream	**0.05**	**Augmented betamethasone dipropionate**	**15, 45 g**
	Lotion	**0.05**	**Augmented betamethasone dipropionate**	**60 mL**
	Olux foam	0.05	Clobetasol propionate	50-, 100-g can
	Olux-E	0.05	Clobetasol propionate	50-, 100-g can
	Psorcon ointment	**0.05**	**Diflorasone diacetate**	**15, 30, 60 g**
	Topicort spray	0.25	Desoximetasone	30, 50, 100 mL
	Vanos	0.1	Fluocinonide	30, 60, 120 g
II	**Ointment**	**0.1**	**Amcinonide**	**60 g**
	Ointment	**0.05**	**Betamethasone dipropionate**	**15, 45 g**
	Cream	**0.05**	**Betamethasone dipropionate**	**15, 45**
	Lotion	**0.05**	**Betamethasone dipropionate**	**60 mL**
	Halog cream	0.1	Halcinonide	15, 30, 60 g
	Halog ointment	0.1	Halcinonide	15, 30, 60 g
	Kenalog ointment	0.5	Triamcinolone acetonide	15 g
	Cream	**0.05**	**Fluocinonide**	**15, 30, 60 g**
	Emollient	**0.05**	**Fluocinonide**	**15, 30, 60 g**
	Gel	**0.05**	**Fluocinonide**	**15, 30, 60 g**
	Ointment	**0.05**	**Fluocinonide**	**15, 30, 60 g**
	Solution	**0.05**	**Fluocinonide**	**60 mL**
	Psorcon cream	**0.05**	**Diflorasone diacetate**	**15, 30, 60 g**
	Topicort cream	**0.25**	**Desoximetasone**	**15, 60, 100 g**
	Topicort gel	**0.05**	**Desoximetasone**	**15, 60 g**
	Topicort ointment	**0.25**	**Desoximetasone**	**15, 60, 100 g**
III	**Cream**	**0.5**	**Triamcinolone acetonide**	**15 g**
	Cutivate ointment	**0.005**	**Fluticasone propionate**	**30, 60 g**
	Lotion	**0.1**	**Amcinonide**	**60 mL**
	Cream	**0.1**	**Amcinonide**	**15, 30, 60 g**
	Cream	**0.05**	**Betamethasone dipropionate**	**15, 45 g**
	Lotion	**0.05**	**Betamethasone dipropionate**	**60 mL**
	Ointment	**0.05**	**Betamethasone dipropionate**	**15, 45 g**
	Elocon ointment	**0.1**	**Mometasone furoate**	**15, 45 g**
	Oral paste	**0.5**	**Triamcinolone acetonide**	**5 g**

Group*	Brand Name or Generic Name†	Drug Strength (%)	Generic Name	Drug Sizes‡
IV	**Cream**	**0.1**	**Amcinonide**	**15, 30, 60 g**
	Elocon cream	**0.1**	**Mometasone furoate**	**15, 45 g**
	Elocon lotion	**0.1**	**Mometasone furoate**	**30, 60 mL**
	Kenalog ointment	**0.1**	**Triamcinolone acetonide**	**15, 80, 453.6 g**
	Luxiq foam	**0.12**	**Betamethasone valerate**	**50-, 100-, 150-g can**
	Synalar ointment	**0.025**	**Fluocinolone acetonide**	**15, 60, 120 g**
	Cream	**0.05**	**Desoximetasone**	**15, 60 g**
	Ointment	**0.05**	**Desoximetasone**	**15, 60 g**
	Westcort ointment	0.2	Hydrocortisone	15, 45, 60 g
V	**Cream**	**0.1**	**Betamethasone valerate**	**15, 45 g**
	Ointment	**0.1**	**Betamethasone valerate**	**15, 45 g**
	Lotion	**0.1**	**Betamethasone valerate**	**60 mL**
	Cloderm cream	0.1	Clocortolone pivalate	45-, 90-g tube
	Cloderm cream	0.1	Clocortolone pivalate	30-, 75-g pump
	Cutivate cream	**0.05**	**Fluticasone propionate**	**30, 60 g**
	Dermatop cream	0.1	Prednicarbate	15, 60 g
	DesOwen ointment	**0.05**	**Desonide**	**60 g**
	Kenalog cream	**0.1**	**Triamcinolone acetonide**	**15, 60, 80, 454 g**
	Kenalog ointment	**0.025**	**Triamcinolone acetonide**	**15, 80 g**
	Kenalog lotion	**0.1**	**Triamcinolone acetonide**	**60 mL**
	Kenalog spray	0.147 mg/g	Triamcinolone acetonide	63-g can, 100-g can
	Locoid Lipocream	**0.1**	**Hydrocortisone butyrate**	**45, 60 g**
	Locoid cream	**0.1**	**Hydrocortisone butyrate**	**15, 45 g**
	Locoid ointment	**0.1**	**Hydrocortisone butyrate**	**15, 45 g**
	Locoid lotion	0.1	Hydrocortisone butyrate	59, 118 mL
	Locoid solution	**0.1**	**Hydrocortisone butyrate**	**60 mL**
	Synalar cream	**0.025**	**Fluocinolone acetonide**	**15, 60, 120 g**
	Westcort cream	0.2	Hydrocortisone	15, 45, 60 g
VI	**Cream**	**0.05**	**Alclometasone dipropionate**	**15, 45, 60 g**
	Ointment	**0.05**	**Alclometasone dipropionate**	**15, 45, 60 g**
	Kenalog cream	**0.025**	**Triamcinolone acetonide**	**15, 80 g**
	Kenalog lotion	0.025	Triamcinolone acetonide	60 mL
	Capex shampoo	0.01	Fluocinolone acetonide	120 mL
	Derma-Smoothe FS	**0.01**	**Fluocinolone acetonide**	**4 oz**
	DesOwen cream	**0.05**	**Desonide**	**60**
	DesOwen lotion	**0.05**	**Desonide**	**59, 118 mL**
	Verdeso foam	0.05	Desonide	50-, 100-g can
	Solution	0.01	Fluocinolone acetonide	60 mL
VII	**Cream**	**2.5**	**Hydrocortisone**	**20, 30, 453.6 g**
	Texacort solution	2.5	Hydrocortisone	30 mL
	Ointment	**2.5**	**Hydrocortisone**	**1 oz**
	OTC	**1.0**	**Hydrocortisone**	**Many brands**
	OTC	**0.5**	**Hydrocortisone**	**Many brands**

*Listed by potency group: group I is the most potent.
†Generic names are given in **boldface** and are listed as cream, ointment, lotion.
‡Many are generics of different sizes.